

Effects of Baduanjin Exercise on Cognitive Function and Cancer-related Symptoms in Women With Breast Cancer Receiving Chemotherapy: a Randomized Controlled Trial

Xiaolin Wei

Fudan University: Obstetrics and Gynaecology Hospital

Ruzhen Yuan

Tongji University Dongfang Hospital

Juan Yang

Shanghai University of Traditional Chinese Medicine Yueyang Hospital of Integrated Traditional Chinese Medicine and Western Medicine

Wei Zheng

Shanghai University of TCM Affiliated Longhua Hospital

Yongmei Jin

Shanghai Seventh People's Hospital

Mingyue Wang

Shanghai University of TCM: Shanghai University of Traditional Chinese Medicine

Jieting Jiang

Shanghai University of TCM: Shanghai University of Traditional Chinese Medicine

Caiqin Wu (✉ yuwuchina@aliyun.com)

Shanghai University of TCM: Shanghai University of Traditional Chinese Medicine

Kunpeng Li

Shanghai University of TCM: Shanghai University of Traditional Chinese Medicine

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Abstract

Purpose Cognitive decline is one of the main side effects of breast cancer patients after relevant treatment, but there is a lack of clear measures for prevention and management without definite mechanism. Moreover, postoperative patients also have a need for limb rehabilitation. Whether the cognitive benefits of Baduanjin exercise can improve the overall well-being of this breast cancer patients remains unknown. This study aims to figure out these problems in the under-researched Chinese population.

Methods This randomized controlled trial was conducted on 70 patients with breast cancer undergoing chemotherapy who were randomly assigned and allocated to (1:1) the supervised Baduanjin group (5 times/week, 30 min each time) or the control group for three months. The effects of Baduanjin exercise intervention were evaluated by outcome measures including subjective cognitive function, symptoms (fatigue, depression and anxiety) and health-related quality of life at pre-intervention (T0), 4 weeks (T1), 8 weeks (T2) and 12 weeks (T3). The collected data were analyzed by using an intention-to-treat principle and linear mixed-effects modeling.

Results Participants in the Baduanjin group had a significantly greater improvement in terms of FACT-cog ($F=14.511$; $P < 0.001$), PCI ($F=15.915$; $P < 0.001$), PCA ($F=2.767$; $P= 0.047$), and health-related quality of life ($F=8.900$; $p = 0.004$) compared with the control group over the time. The exercise-cognition relationship was significantly mediated by reduced fatigue (indirect effect: $\beta= 0.132$; 95% CI: 0.046, 0.237) and improved anxiety (indirect effect: $\beta=-0.075$; 95% CI: -0.165, -0.004).

Conclusions This pilot study revealed the benefits and outlined the underlying mediating mechanism of Baduanjin exercise to the subjective cognition and health-related quality of life of Chinese breast cancer patients receiving chemotherapy. The findings provided insights into the development of public health initiatives to promote brain health and improve quality of life among breast cancer patients.

Trial registration number ChiCTR 2000033152

Introduction

Cognitive impairment in cancer patients is mostly attributed to cancer and treatment, including chemotherapeutic agents, hormone therapy, and radiation therapy, which is also known as cancer-related cognitive impairment (CRCI) [1]. CRCI is predominately characterized by the change of memory, processing speed, attention or concentration, and executive function [2, 3], which manifests during or post-treatment with variable degrees, onset and duration. Up to 75% of cancer patients have been reported accompanied by mild to severe cognitive complaints, which can persist for months to even few years after the completion of treatment [4]. Cognitive complaints are the most frequent complication reported by breast cancer (BC) patients [5] that more than 50% of these patients following chemotherapeutic drugs exist; however, only 15%-25% of these cancer patients have shown poor performance in objective cognition [6]. These BC patients may experience difficulties in daily functioning,

decision-making, multitasking and word retrieval, and treatment adherence; thereby, CRCI has become one of the prevalent factors that compromise the quality of life and decreased survival [7].

As the exact underlying mechanisms and etiologies of CRCI are still unclear, recent studies have emerged proposing several candidates. Affected cancer patients showed increased levels of C-reactive protein (CRP), tumor necrosis factor alpha, Interleukin-6 [8–11]. Meanwhile, the serum levels of Interleukin-1 receptor antagonist and Interleukin-10 were decreased [11]. At the same time, other underlying mechanisms were found, included chemotherapy-induced neurotoxicity, decreased hippocampal neurogenesis, white matter abnormalities, and increased oxidative stress [12]. In addition, pervasive fatigue and negative emotions may contribute to increased susceptibility of cognitive impairment. There was a moderate positive correlation between subjective cognitive impairment and fatigue in postmenopausal breast cancer patients [13]. The study found that BC patients undergoing systemic treatment had higher levels of fatigue and more subjective cognitive problems along with the decline of executive function [14]. The result [15] showed that the subjective cognitive function of BC patients after 6 months of chemotherapy was significantly lower than before chemotherapy, and there was a significant correlation with anxiety and depression. However, there is also a contradictory result that the association between cognitive impairment and depression didn't exist [16].

There is currently a high need for therapeutic interventions that can reduce cognitive complaints. Exercise is an established safe and effective therapy for managing adverse effects of cancer treatment, including fatigue, psychological distress, functional decline, and detrimental body composition changes [17–19]. Accumulating evidences on the exercise on positively improving cognitive function in healthy older adults and those with mild cognitive impairment or more severe neurocognitive impairment (i.e., AD, stroke) have sparked significant interest in the potential use of exercise as a management strategy for CRCI [20, 21]. A vast number of studies have shown that moderate-to-vigorous physical activity can certainly mitigate or ameliorate cognitive impairment in BC patients, especially in processing speed, executive function, working memory, etc. [22–24]. Two pilot studies showed that aerobic exercise improved objective cognition. One study [23] found that a 12-week exercise intervention improved the processing speed, but there was no significant improvement in self-reported cognitive function. Another study showed that a 24-week supervised and home-based aerobic exercise program demonstrated similar results in postmenopausal women with early-stage breast cancer [25]. Nevertheless, one contradictory study [26] showed that aerobic exercise plus resistance training improved subjective cognitive function. Unfortunately, due to limited preclinical studies and testing, evidence-based recommendations are insufficient. Thereby, more rigorous studies need to be warranted.

Baduanjin, as a kind of exercise therapy based on mindfulness, such as Qigong and Taichi, is a combination of breathing and exercise, which is beneficial for fatigue, quality of life, and negative mood among patients [18, 19]. Regular Baduanjin exercise can improve the cognitive function of the old people with mild cognitive impairment. Of course, there are also studies concerning medical Qigong to improve the cognitive function of BC patients. The results of study [27] showed that Qigong improved the self-

cognition function, executive function and language fluency. In light of higher withdrawal rate and poor adherence in this study, the effect of exercise on cognitive functioning needs further explanation.

Therefore, the primary purpose of this study is to determine whether Baduanjin exercise programme is a protective measure for cognitive decline in chemotherapy-exposed patients with early-stage breast cancer. Moreover, this study aims to examine whether or not cancer-related symptoms (fatigue, depression and anxiety) and quality of life are improved and its possible association.

Methods

Study design and setting

This was a single-blinded randomized controlled trial with two study arms, including a supervised Baduanjin exercise group and a wait-list control group. Participants were recruited from the three affiliated hospitals of Shanghai University of Traditional Chinese Medicine, including Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Seventh People's Hospital, and Longhua Hospital. The outcome measures were evaluated in a quiet room in the hospital to avoid interference.

Participants

Participants were randomly assigned to an intervention group or a control group—in a 1:1 ratio using SPSS 24.0 software. Researchers screened patients who met the inclusion and exclusion criteria and provided relevant information, as well as possible benefits of the exercise and the safety. After obtaining consent, the research team examined the candidates with patients' questionnaire. The inclusion criteria were showed as follows: (1) female patients newly diagnosed with stage I to III breast cancer; (2) scheduled to receive adjuvant chemotherapy; (3) aged 40 to 75 years; (4) using WeChat; (5) sufficient fluency of the Chinese language; (6) willing to participate in the study and be randomly assigned. Exclusion criteria included participants with (1) disease recurrence or metastasis; (2) known conditions and/or diseases that impact cognition (e.g., Alzheimer's disease, dementia, or other psychological diagnoses); (3) disorders that might preclude exercise participation (e.g., fracture, arthritis); (4) current participation in mindfulness-based exercise programs (e.g., TaiChi or Qigong). Due to the nature of exercise studies, only results evaluators were blinded. More details were presented in this previous protocol of study [28].

Sample size estimation

The sample size was estimated in this study by using perceptible cognitive impairment as the main effect indicator, which refers to the results of previous study [29]. Using the G*Power 3.1 software, 58 cases of the total sample were calculated with a test power of 0.80. Considering the 20% dropout rate, the total sample size for this study was about 70 patients randomized to the intervention group or the control group.

Study interventions

Baduanjin exercise

Baduanjin exercise was conducted according to the standards promulgated by the General Administration of Sport in China in 2003. A professionally trained Qigong specialist uniformly trained subject researchers to learn the exercise training. Researchers then conducted on-site instruction to guide these participants and correct their movements. Participants also were provided with video demonstration to promote daily practice. Before initiating the first cycle of chemotherapy, the patients had the first session in the hospital, then following the video workout at home. Recommended training time was 5 times a week for half an hour each time during the 12-week exercise period. The program began with stretching the joints, inhalation and exhalation for 2 min respectively, and two 12 min Baduanjin sessions, followed by 2 min of muscle relaxation exercises. Each patient's log was recorded during exercise at home, including any obstacles that affected exercise training. When the patient went to the hospital to receive the next cycle of chemotherapy, the feedback of exercise log was collected and checked.

Control intervention

Patients randomized to the control group were given a face-to-face health education. Disease-related questions raised by the patients were directly communicated or answered through WeChat online or oral communication. Patients improved the affected limb through exercises, including abduction, forward flexion, backward extension, internal rotation, and wall climbing according to the guideline and standard for the diagnosis and treatment of breast cancer in China [30]. In addition, the patients were not asked to conduct other aerobic activities. Researchers asked about their conditions twice a week during the 12 weeks.

Measurement

Socio-demographic profile

At baseline, a self-designed demographic data sheet was used to collect the social-demographic data, including age, BMI, marital status, income, education and living condition, as well as relevant disease information from electronic medical system.

Outcome measurement

The Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog) was developed by Wagner et al [31] to assess subjective cognitive function. The Chinese versions of the FACT-Cog was used; The Multidimensional Fatigue Symptom Inventory-short form (MFSI-SF) was used to assess the fatigue of patients in multiple aspects [32]. Taiwanese scholar then revised the Chinese version of the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF-C) [33], which was used in this study; The Hospital Anxiety and Depression Scale (HADS) was used for the assessment of patients' anxiety and depression [34]; The Functional Assessment of Cancer Therapy-Breast (FACT-B), a 44-item self-report

instrument was well-known and widely used to measure multidimensional quality of life (QoL) in patients with breast cancer [35].

Procedure and ethical considerations

The protection of human subject was approved by the Ethics Committee of the Seventh People's Hospital of Shanghai University of Traditional Chinese Medicine (No. 2020-7th-HIRB-011). The purpose and process were explained to potential participants. Written informed consent was obtained from each participant; each participant was assured of confidentiality and the option to decline participation or to withdraw from the trial at any time without penalty. Baseline data collection was conducted by two trained research assistants. After the pre-test data collection, the participants were randomly allocated to receive the Baduanjin exercise programme or the wait-list control group. The post-test data was collected at 4 weeks (T1), 8 weeks (T2), and 12 weeks (T3) during intervention.

Data analysis

Demographics and other characteristics were reported descriptively via the statistics software (SPSS 24.0). The means and SD were calculated for continuous normally distributed variables and medians and ranges for non-normally distributed variables. Categorical variables were presented by absolute numbers and percentages. We performed complete case analyses after describing the pattern of missing data.

According to the intention-to-treat principle, a linear mixed-effect model for repeated-measures analysis was used, in which group, time point, and the interaction between group and time point were set as fixed effects; individual patient was set as the random effects; and age was adjusted as a covariate in the model. Adherence to the Baduanjin exercise was noted. Two-sided significance level for all tests was 0.05. The PROCESS macro [36] was employed to examine the mediating effects of fatigue and anxiety on the relationship between the exercise and subjective cognition. 95% confidence intervals for direct and indirect effects were generated via bias-corrected bootstrapping with 10,000 resamples. The nonparametric bootstrapping procedures are superior to traditional regression methods for testing the mediating effects, because the former does not make assumptions regarding the shape of the distribution of the variables or the sampling distribution [37]. Confidence intervals without zero showed significant mediation.

Results

Recruitment

As shown in the CONSORT flow diagram (Fig. 1), 107 BC patients were approached for eligibility screening. Among the 70 participants who met the selection criteria and consented to participate. During the study period, according to the results of exercise diary, 24 of the 35 patients (80%) had a completion rate > 85%, which could be considered as good compliance, mainly because of severe diarrhea after

chemotherapy (n=1) or voluntarily withdrew (n=2). No adverse events, such as lymphedema related to exercise, occurred.

Participant characteristics

The median age of the included patients was 55 (46, 60), with the majority married and relatively low-educated (52.9% indicating they had a junior high school education or less). 68.6% of the patients were menopausal. The majority of participants were early breast cancer patients (stage I-II) with 50% in stage II. Anthracyclines accounted for 51.4% in all chemotherapy regimens, and non-anthracyclines for 48.6%; 7.1% chemotherapy regimen combined with targeted therapy; breast cancer patients with comorbidities accounted for 24.3%. The demographic and clinical disease characteristics of the participants were shown in Table 1. No considerable difference was observed between groups at baseline.

Effects on cognitive function

At the 4th, 8th, and 12th weeks, FACT-Cog scores of both groups are presented in Table 2. Participants in the Baduanjin group had significantly greater improvement in their FACT-cog score compared with the wait-list control group across the baseline and post-intervention periods ($F=19.456$; $P< 0.001$). Amongst all the subscales of FACT-cog, the results were significant for PCI ($F=15.915$; $P< 0.001$), PCA ($F=2.767$; $P= 0.047$), the impact of cognition on the quality of life ($F=9.410$; $P= <0.001$), and no significant difference was found in evaluation of others ($F=3.766$; $P= 0.056$).

Effects on health-related quality of life

At the 4th, 8th, and 12th weeks, FACT-B scores of both groups are presented in Table 3. Participants in the intervention group were found to have a significantly greater improvement in FACT-B score compared with the wait-list control group across the baseline and post-intervention periods ($F=8.900$; $P=0.004$). Amongst the FACT-B items, the mixed-effect modeling results were significant for physical well-being ($F=4.908$; $P=0.03$), emotional well-being ($F=7.640$; $P= 0.007$) (Supplementary Table 2). No significant difference was shown in terms of social/family function, functional well-being and additional attention ($F=3.766$; $P= 0.056$). The scores of the FACT-B and Constant-Murley scores in both groups of breast cancer patients were improved, but the baduanjin group was significantly better than the control group (see supplementary material).

Results of the mediating analysis

Through linear regression analysis, the FACT-cog score had a linear correlation with fatigue score ($\beta=-0.392$, $P<0.001$), and it had a linear correlation with anxiety score ($\beta = 0.339$, $P=0.001$). There was no correlation between FACT-cog score and depression score ($\beta=-0.053$, $P=0.585$). On this basis, a mediation hypothesis model of fatigue and anxiety is established. After putting fatigue and anxiety into intermediary variables through SPSS PROCESS, the result analysis of the intermediary model is shown in Fig. 2. Exercise has a negative effect on anxiety ($\beta=-0.795$, $t=-2.105$, $P<0.05$); exercise has a significant negative effect on fatigue ($\beta=-0.733$, $t=-3.319$, $P<0.001$); It has a significant positive effect on cognition (β

= 5.875, $t=5.932$, $P<0.001$); fatigue has a significant negative effect on subjective cognitive ability ($\beta=-1.618$, $t=-4.432$, $P<0.001$). It shows that exercise can not only directly affect the improvement of subjective cognition, but also improve subjective self-cognition by reducing fatigue and anxiety. The direct effect and the mediating effect of fatigue and anxiety accounted for 50.00%, 18.57%, and 10.59% of the total effect, respectively.

Discussion

The aim of this study is to investigate the effects of a 12-week Baduanjin exercise on cognitive function, cancer-related symptoms and quality of life in BC patients during chemotherapy, and the exercise-cognition relationship. This study echoes the cognitive-enhancing benefits of other aerobic and mind-body exercise amongst breast cancer population. This study showed that exercise training can meet the treatment goal of preventing the deterioration of cognitive function among BC patients. By incorporating a mediating analysis, this study adds further evidence to indicate that cognitive benefits of physical exercise are manifested through its positive effects on two cognitive risk factors, including fatigue and anxiety. This exercise intervention may alleviate the effect of cognitive decline on the overall well-being of BC patients.

Cognitive benefit of exercise

The subjective feelings of cancer patients are the most relevant measure of clinical significance, and the self-reported cognition of patients should be used as the main outcome indicator for CRCI. The results showed that the subjective cognitive ability and PCI of the patients in the Baduanjin group were significantly better than those in the Baduanjin group at 8 and 12 weeks. However, no obvious significance was found between groups at the 4th week, which may be attributed to the patients in the exercise adaptation period. In addition, BC patients were in the initial postoperative recovery period, and their postures for exercise cannot be fully standardized. This was similar to the results of Myers et al [27], who divided the BC patients into the Qigong group, the general exercise group and the wait-list control group for 8 weeks intervention. The results showed that the PCI and PCA in the Qigong group were significantly improved compared with the wait-list control group. Another randomized controlled study [29] also conducted a 10-week medical Qigong intervention, and the results showed that the Qigong group's subjective cognitive ability and PCI were improved. Baduanjin exercise has a certain preventive effect on the decline of subjective cognitive ability of breast cancer patients during chemotherapy, and the continuous effect of Baduanjin intervention on cognitive ability after the end of the 12-week Baduanjin intervention has not been observed due to personnel and time constraints, which can be further observed in future large sample studies.

Effects of exercise on health-related quality of life

BC patients were attributed to cancer, cancer treatment, or combined with other diseases, developing long-term physical and psychological diseases, such as fatigue, sleep disturbance, mood, etc. Studies have shown that these patients with less education, comorbidities, and chemotherapy were more likely to

possess poor quality of life, while lack of social support and unmet needs may lead to poor health-related life [38]. Baduanjin exercise improved quality of life among BC patients at the 8th and 12th week. In addition, this study also showed that the shoulder joint function in both groups was improved at the 8th and the 12th week, indicating that Baduanjin was beneficial to promote the recovery of the shoulder joint function, especially the active range of movement of the shoulder joint. These results were consistent with the results of Ying et al [18]. After 6 months of Baduanjin intervention, patients in the Baduanjin group had significantly improved in shoulder joint mobility, and quality of life. At the same time, another randomized controlled trial [39] also found that after 12 weeks of Baduanjin intervention, the quality of life of patients in the Baduanjin group was better than that of the control group. The anxiety and depression symptoms of the two groups were improved, but the difference between the groups was not statistically significant, and the quality of life was positively correlated with anxiety and depression. The above results indicated that Baduanjin intervention has a certain effect on improving the quality of life of breast cancer patients during chemotherapy. In addition, studies have also shown that Baduanjin had an effect on increasing BMI, relieving postoperative limb pain and lymphatic swelling [40], but significant differences in BMI and pain between the two groups was not observed in this study. The possible reason may be that most of the patients' surgical methods were lymphatic dissection, but most of them were sentinel dissection. Axillary dissection was relatively small, and some BC patients underwent breast-conserving surgery, without obvious postoperative pain. Secondly, lymphedema generally appeared in 3 to 6 months after the operation, and no obvious limb swelling was found in the two groups of patients during the intervention period. Therefore, a 3-month follow-up after the end of the intervention can be done to observe the changes in future studies.

Anxiety symptoms and fatigue mediated the exercise–cognition relationship

Subjective cognitive impairment has been associated with poor physical function, anxiety, depression and fatigue, which was more likely to occur in cancer patients and even worsen [41]. Baduanjin can improve the physical function and mental health [19]. A longitudinal observational study found that fatigue played a role between physical activity and subjective cognition [42]. Another study [43] showed that the severity of cognitive impairment increased with the degree of insomnia in postmenopausal BC patients. Sleep disturbance may also be an influencing factor for CRCI, but we did not follow up the sleep quality. In addition, Song et al [44] showed that aerobic exercise improved the quality of sleep and reduce depression in elderly people with mild cognitive impairment. Physical activity affected cognition including increasing the level of BDNF in plasma, improving metabolic function, and reducing systemic inflammation [45]. The level of BDNF was related to processing speed, increasing significantly after aerobic exercise [46]. Future research may further explore the changes in cognitive function, such as brain tissue and its function, immunohistochemistry, etc., to contribute to the mechanism of exercise to improve cognitive function, and it needs to be further determined whether the management strategy of CRCI can be improved by solving fatigue, anxiety or sleep problems.

Limitations

This study has several limitations. Firstly, this study took into account the research characteristics of exercise intervention, and it was impossible to blind the subjects and Baduanjin practitioners, but only blinded the outcome assessors. Secondly, although the neuropsychological test used in the evaluation was relatively mature in clinical application, it cannot completely avoid the subjective influence of the test. Although some movements were gradually trained, the initial movements were still different from the original standardized movements, so the results could be influenced to a certain extent. In addition, the sample size is not large, and the interpretation of the results has certain limitations. A larger sample can be considered in the next study. Finally, taking into account the issue of research funding, we didn't collect the laboratory indicators related cognition, which may be included as part of mechanism research in the future, and the effects of exercise on CRCI can be further enriched through multidisciplinary cooperation.

Conclusion

This study presented a positive scenario of a 12-week group based on Baduanjin exercise for protection of the cognitive decline and improvement of quality of life among BC patients receiving chemotherapy. Furthermore, decreasing anxious and improving fatigue were firstly identified as part of the possible mechanisms underlying the exercise-cognition relationship. The effectiveness and feasibility of this exercise also promoted the need to increase its application against further cognitive decline in BC patients.

Declarations

Acknowledgements

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Availability of data and material

These data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Code availability

N/A.

Author contribution

Conceptualization, Methodology: [Wu Caiqin]c; Data curation, Writing-Original draft preparation: [Wei Xiaolin]; Visualization, Investigation: [Jiang Jieting], [Wang Mingyue]; Supervision: [Yang juan], [Jin Yongmei], [Zheng wei]; Software, Validation: [Yuan Ruzhen]; Writing- Reviewing and Editing: [Li Kunpeng]. All authors read and approved the final manuscript.

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Ethics approval

The study received ethical approval from the Ethics Committee of the Seventh People's Hospital of Shanghai University of Traditional Chinese Medicine (No. 2020-7th-HIRB-011).

Consent to participate

All participants provided informed consent prior to enrolling onto the study.

Consent for publication

All authors consent to the publication of this manuscript in Supportive Care in Cancer.

Conflict of interest

None.

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Tables

Table 1 Comparison of demographic and baseline characteristics.

Characteristic	Overall (n=70)	Intervention group (n=35)	Control group (n=35)	t/z/ χ^2	P
Age, y, median (range) [#]	55[46~60]	52[43~60]	55[50~62]	-0.912	0.362
BMI, mean \pm SD	23.06 \pm 2.54	22.86 \pm 2.55	23.26 \pm 2.56	-0.645	0.521
Educational level, n (%) [#]				-0.704	0.481
Middle school or less	37[52.9%]	17[24.3%]	20[28.6%]		
High school	19[27.1%]	10[14.3%]	9[12.9%]		
College	13[18.6%]	8[11.4%]	5[7.1%]		
Postgraduate	1[1.4%]	0[0%]	1[1.4%]		
Marriage, n (%)				0.355	0.837
Single	3[4.3%]	1[1.4%]	2[2.9%]		
Married	65[92.9%]	33[47.1%]	32[45.7%]		
Widowed	2[2.9%]	1[1.4%]	1[1.4%]		
Employment status, n (%)				1.228	0.541
Retired	27[38.6%]	13[18.6%]	14[20.0%]		
Employed	20[28.6%]	12[17.1%]	8[11.4%]		
Unemployed	23[32.9%]	10[14.3%]	13[18.6%]		
Monthly household Income [RMB], n (%) [#]				-0.977	0.328
[1000	2[2.9%]	1[1.4%]	1[1.4%]		
1000~2000	4[5.7%]	3[4.3%]	1[1.4%]		
2000~3000	17[24.3%]	10[14.3%]	7[10.0%]		
3000~5000	18[27.1%]	8[11.4%]	10[15.7%]		
[5000	29[40%]	13[18.6%]	16[21.4%]		
Menopausal status, n (%)				1.061	0.303
Pre-menopausal	22[31.4%]	13[18.6%]	9[12.9%]		
Post-menopausal	48[68.6%]	22[31.4%]	26[37.1%]		
BC stage, n (%) [#]				-0.202	0.840
I	27[38.6%]	13[18.6%]	14[20.0%]		
II	35[50%]	18[25.7%]	17[23.4%]		

	8 (11.4%)	4 (5.7%)	4 (5.7%)		
Type of surgery, n (%)				3.530	0.171
Lumpectomy	12 (17.1%)	6 (8.6%)	6 (8.6%)		
Quadrantectomy	23 (32.9%)	8 (11.4%)	15 (21.4%)		
Mastectomy	35 (50%)	21 (30.0%)	14 (20.0%)		
Chemotherapy regimens, n (%)				3.660	0.056
Anthracycline-based	36 (51.4%)	22 (31.4%)	14 (20.0%)		
Taxane-based	34 (48.6%)	13 (18.6%)	21 (30.0%)		
Combined targeted therapy, n (%)				<0.001	1.000
No	65 (92.9%)	33 (47.1%)	32 (45.7%)		
Yes	5 (7.1%)	2 (2.9%)	3 (4.3%)		
Comorbidity, n (%)				0.324	0.569
Yes	17 (24.3%)	9 (12.9%)	8 (11.4%)		
No	53 (75.7%)	26 (37.1%)	27 (38.6%)		
Patient-reported outcomes					
FACT-Cog, mean (SD)		124.34±8.77	123.31±8.37	0.502	0.617
PCI		70.11±5.05	69.23±5.08	0.731	0.467
PCA		25.60±1.88	25.94±1.75	-0.790	0.432
FACT impact on QOL		13.86±1.54	13.37±1.57	-1.562	0.118
FACT comments from others		14.77±1.42	14.77±1.37	-0.155	0.877
Fatigue MFSI-SF-C, mean (SD)		5.01±1.92	4.77±1.98	0.513	0.610
Anxiety HASD-A, mean (SD)		5.63±2.24	5.97±2.78	-0.231	0.817
Depression HASD-D, mean (SD)		6.14±2.56	6.11±2.61	0.046	0.963
QOL FACT-B, mean (SD)					

Abbreviations: BC, breast cancer; SD, standard deviation; FACT-Cog, Functional Assessment of Cancer Therapy–Cognitive Function; PCA, perceived cognitive abilities; PCI, perceived cognitive impairments;

MFSI-SF-C, Chinese version of the Multidimensional Fatigue Symptom Inventory-Short Form; HASD, Hospital Anxiety and Depression Scale; QOL, quality of life.

P values for between-group differences were calculated using the Mann - Whitney U test.

Table 2 The comparison of subjective cognition between the intervention and control groups.

	Intervention group	Control group	Time effect		Group effect		Group*time effect	
			F	P	F	P	F	P
FACT-cog scores								
T0	124.34±8.77	123.31±8.37	19.456	<0.001	14.511	<0.001	23.589	<0.001
T1	121.29±8.57	117.51±8.15						
T2	122.56±7.65	114.31±7.05						
T3	125.50±7.62	113.00±6.94						
PCI								
T0	70.11±5.05	69.23±5.08	15.915	<0.001	15.789	<0.001	19.842	<0.001
T1	68.11±4.96	65.94±5.12						
T2	68.97±4.54	64.11±4.01						
T3	70.69±4.28	63.46±4.16						
PCA								
T0	25.60±1.88	25.94±1.75	2.767	0.047	6.261	0.015	5.631	0.002
T1	24.80±2.00	24.71±1.58						
T2	25.21±1.72	24.20±1.76						
T3	25.82±1.68	23.91±1.76						
evaluation of others								
T0	14.77±1.42	14.77±1.37	3.766	0.056	9.359	<0.001	11.229	<0.001
T1	14.83±1.18	14.29±1.43						
T2	14.75±1.06	14.06±1.33						
T3	15.22±0.73	14.03±1.18						
Impact on QoL								
T0	13.86±1.54	13.37±1.57	9.410	<0.001	17.428	<0.001	7.548	<0.001
T1	13.54±1.70	12.57±1.48						
T2	13.62±1.60	11.94±1.57						
T3	13.77±1.86	11.49±1.90						

Table 3 The comparison of quality of life between the intervention and control groups.

	Intervention group	Control group	Time effect		Group effect		Group*time effect	
			F	P	F	P	F	P
Fatigue								
T0	5.01±1.92	4.77±1.98	45.453	<0.001	7.723	0.007	4.627	0.004
T1	2.87±1.30	3.64±1.83						
T2	2.06±1.21	3.42±1.68						
T3	1.95±0.85	2.99±1.51						
Anxiety								
T0	5.63±2.24	5.97±2.78	78.453	<0.001	3.714	0.058	1.255	0.291
T1	2.37±2.38	2.94±2.84						
T2	0.83±0.98	2.34±2.56						
T3	0.76±1.23	1.60±2.19						
Depression								
T0	6.14±2.56	6.11±2.61	58.321	<0.001	4.581	0.036	3.590	0.016
T1	3.80±2.35	3.83±2.18						
T2	1.57±1.08	3.26±2.55						
T3	1.25±1.27	2.66±2.21						
Quality of life								
FACT-B scores								
T0	93.55±8.49	93.89±10.70	74.219	<0.001	8.900	0.004	8.248	<0.001
T1	100.57±7.30	99.89±10.20						
T2	110.87±8.53	101.66±8.23						
T3	113.26±6.25	106.17±6.72						
physiological status								
T0	19.89±2.45	20.37±3.02	12.023	<0.001	4.908	0.030	2.757	0.045
T1	22.00±2.59	21.26±3.41						
T2	23.69±5.08	21.63±2.33						
T3	23.33±1.75	21.74±2.43						
social family status								

T0	22.12±1.27	21.46±1.82	38.915	<0.001	1.798	0.184	0.769	0.513
T1	19.26±3.01	19.23±2.70						
T2	21.22±2.38	20.43±2.42						
T3	22.12±1.27	21.46±1.82						
T0	16.71±2.86	17.20±2.80	46.561	<0.001	7.640	0.007	5.633	0.001
T1	19.77±1.65	19.29±2.79						
T2	21.37±1.73	19.51±2.59						
T3	21.84±1.68	19.71±2.05						
functional status								
T0	10.23±3.34	10.91±4.49	82.301	<0.001	3.811	0.055	5.020	0.002
T1	14.86±2.86	15.11±3.51						
T2	18.70±2.48	15.86±2.96						
T3	19.26±3.06	17.49±2.56						
additional attention								
T0	24.60±3.01	23.94±3.59	6.180	<0.001	2.354	0.130	1.659	0.179
T1	24.69±3.46	25.00±3.30						
T2	26.71±2.92	25.77±2.56						
T3	26.71±2.92	25.77±2.56						

Supplementary Tables

Supplementary Tables are not available with this version.

Figures

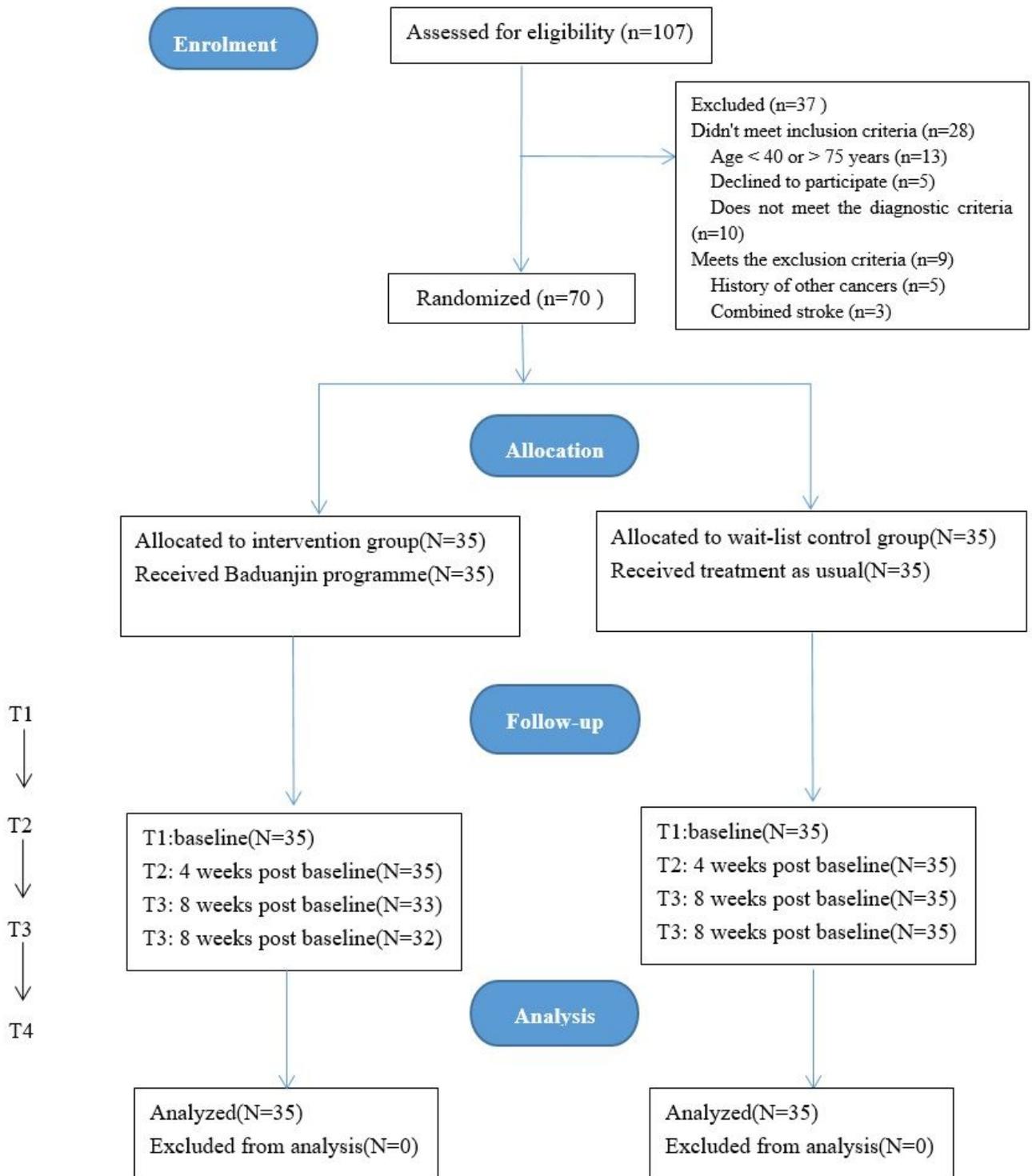


Figure 1

The flow diagram of the recruitment and randomization processes for the current study.

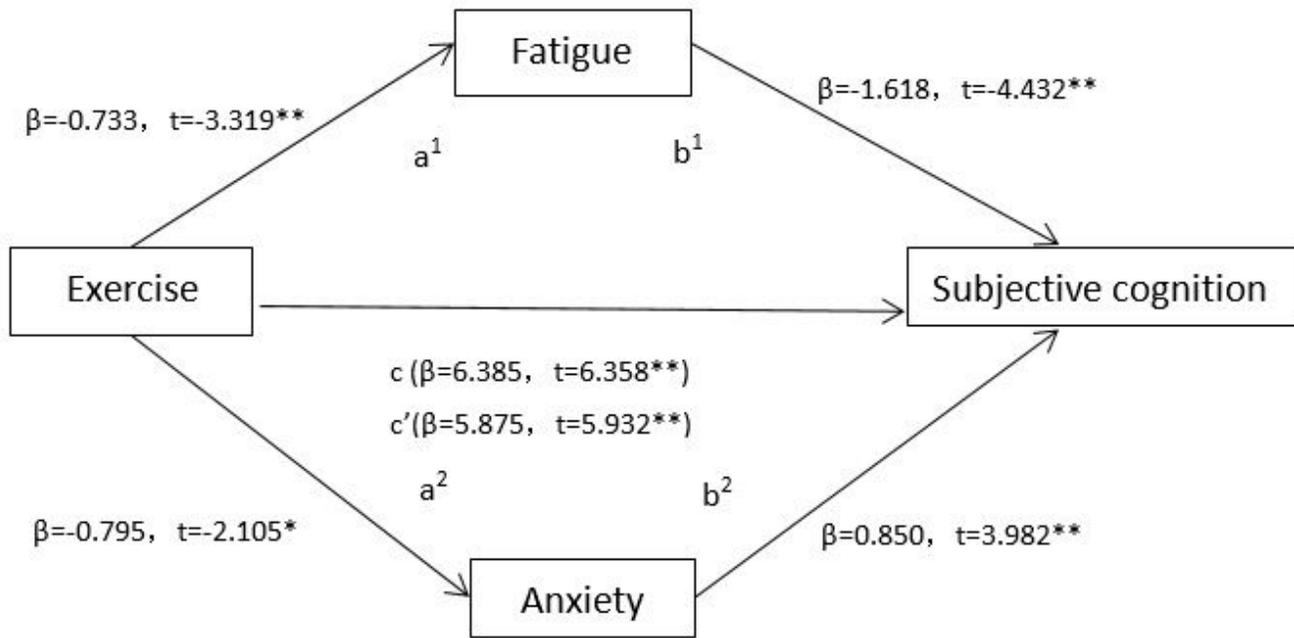


Figure 2

Mediating roles of fatigue and anxiety in the relationship between the Baduanjin exercise and the cognitive changes.

Supplementary Files

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