

Original Research Article

Xiaohui Hou, Hao Lan, Li Cai, Kun Wang, Jingwen Liao* and Min Hu*

Baduanjin exercise for menopausal symptoms in breast cancer patients on aromatase inhibitors: a randomized controlled pilot study

<https://doi.org/10.1515/teb-2025-0015>

Received May 19, 2025; accepted September 18, 2025;

published online September 30, 2025

Abstract

Objectives: This randomized controlled pilot study aimed to investigate the therapeutic effects of Baduanjin exercise – a traditional Chinese mind-body practice integrating gentle movements, diaphragmatic breathing, and mindfulness – on alleviating aromatase inhibitor-induced menopausal symptoms, reducing cancer-related fatigue, and modulating systemic inflammatory markers (IL-6, IL-1 β , TNF- α) in breast cancer patients.

Methods: 70 patients undergoing aromatase inhibitor therapy were recruited from Guangdong General Hospital and randomly assigned to either a Baduanjin exercise group (n=35) or a usual-care control group (n=35). The Baduanjin exercise group completed a supervised 12-week Baduanjin exercise regimen (three sessions weekly, 90 min/session), while controls maintained habitual activity. Menopausal symptoms were assessed using the Kupperman Index, fatigue severity via the Piper Fatigue Scale, and serum inflammatory markers (IL-6, IL-1 β , TNF- α) through enzyme-

linked immunosorbent assays at baseline and post-intervention.

Results: 39 participants (55.7 %) completed the trial (intervention: n=24; control: n=15). The Baduanjin exercise group demonstrated significant reductions in arthralgia severity ($p<0.05$) and fatigue subdomains (affective: $p<0.05$; cognitive/mood: $p<0.05$) compared to controls. Notably, IL-6 levels increased significantly in the Baduanjin exercise group vs. the control group ($p<0.05$), while IL-1 β and TNF- α showed no intergroup differences.

Conclusions: Baduanjin exercise may ameliorate aromatase inhibitor-induced menopausal symptoms and fatigue in breast cancer patients, with distinct modulations in inflammatory biomarkers. Its low-intensity, culturally tailored design supports feasibility as an adjunctive therapy, warranting further investigation into IL-6-mediated mechanisms.

Keywords: Baduanjin exercise; breast cancer; menopausal symptom; cancer-related fatigue; inflammatory biomarkers

Introduction

Breast cancer is the most prevalent malignancy among women globally and the leading cause of cancer-related morbidity in China [1]. Advances in multimodal therapies, including surgery, endocrine therapy, and targeted treatments, have significantly improved survival rates, particularly for hormone receptor-positive cases, which constitute over 50 % of diagnoses [2–4]. Aromatase inhibitors, as a core treatment modality for adjuvant endocrine therapy in postmenopausal hormone receptor-positive breast cancer patients, reduce the overall recurrence risk by 27 % compared with no extended treatment after the initial 5-year therapy, underscoring their long-term recurrence prevention value [5]. However, their clinical benefits are negated by a high discontinuation rate (36.9 % within five years) due to treatment-emergent adverse effects such as arthralgia, vasomotor symptoms, and fatigue, which impair quality of life and increase mortality risk among non-adherent patients [6, 7].

Xiaohui Hou and Hao Lan these authors have contributed equally to this work.

*Corresponding authors: **Jingwen Liao**, PhD, Guangdong Provincial Key Laboratory of Physical Activity and Health Promotion, Guangzhou Sport University, Guangzhou, China, E-mail: liaojw@gzsport.edu.cn; and

Min Hu, PhD, Department of Sports and Health, Guangzhou Sport University, Guangzhou, China; and Guangdong Provincial Key Laboratory of Physical Activity and Health Promotion, Guangzhou Sport University, Guangzhou, China, E-mail: minhu@gzsport.edu.cn

Xiaohui Hou and Hao Lan, Department of Sports and Health, Guangzhou Sport University, Guangzhou, China; and Guangdong Provincial Key Laboratory of Human Sports Performance Science, Guangzhou Sport University, Guangzhou, China

Li Cai, Department of Martial Arts, Guangzhou Sport University, Guangzhou, China

Kun Wang, Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital, Guangzhou, China

Non-pharmacological interventions, particularly exercise, are increasingly recognized for mitigating therapy-related toxicities. Aerobic and resistance training demonstrate efficacy in reducing symptoms, yet their high-intensity protocols often exclude patients with functional limitations or comorbidities [8–11]. In contrast, Baduanjin exercise – a traditional Chinese mind-body exercise that integrates gentle, rhythmic movements, diaphragmatic breathing, and mindfulness meditation – offers a low-intensity, accessible alternative [12–14]. Preliminary evidence suggests its potential in alleviating cancer-related fatigue and modulating inflammatory pathways [15–17], but rigorous evaluation in aromatase inhibitor-treated populations remains lacking. This single-center randomized controlled pilot study focused on verifying intervention feasibility and preliminary efficacy.

Breast cancer patients treated with aromatase inhibitors frequently experience persistent menopausal-like symptoms (e.g., fatigue, hot flashes, arthralgia), which reduce treatment adherence and impair quality of life (QOL). For QOL assessment in this population, existing studies using standardized questionnaires have confirmed a significant burden: the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) shows patients have notably lower scores in physical function, emotional function, and global QOL, with physical discomfort scores negatively correlated with treatment adherence [18–20]; the Functional Assessment of Cancer Therapy-Endocrine Symptoms (FACT-ES) (designed for endocrine therapy populations) accurately captures the interference of aromatase inhibitor – specific symptoms (e.g., joint pain, hot flashes) on QOL, where the magnitude of score reduction is directly associated with symptom severity [21–23]; the Breast Cancer-Specific Module 23 (BR23) reveals disease-specific concerns (e.g., body image distress, fear of recurrence) further exacerbate QOL impairment [24–26]. Thus, based on the existing evidence, we suggest that future exercise intervention studies for this group consider including these three questionnaires pre- and post-intervention to allow for a comprehensive evaluation of QOL improvements. While exercise interventions are increasingly recommended to manage therapy-related side effects, evidence shows that regular physical activity across various forms effectively alleviates menopause-associated symptoms [27, 28]. Existing protocols, however, primarily focus on aerobic or resistance training, which may not adequately accommodate the functional limitations common in this population. The aim of this randomized controlled pilot study was to first verify the feasibility of a 12-week supervised Baduanjin program in this cohort, and second, to explore its preliminary efficacy in alleviating

menopausal-like symptoms (assessed via the Kupperman Index and Piper Fatigue Scale) and modulating serum inflammatory biomarkers among patients treated with aromatase inhibitors. The summary of this article is presented in Figure 1. By integrating culturally rooted, low-intensity exercise with objective biomarker analysis, this study sought to address critical gaps in current supportive care strategies, particularly how mind-body exercises distinct from conventional aerobic or resistance training may regulate inflammation to improve symptom outcomes [29, 30]. Such insights could inform tailored interventions to enhance therapeutic adherence and survivorship experiences in breast cancer patients treated with aromatase inhibitors.

Materials and methods

Study design

This single-center randomized controlled pilot study was implemented at Guangdong Provincial People's Hospital following Ethical Approval from the Institutional Review Board of Guangdong General Hospital (Approval No. GDREC2016424H-R1). The research protocol strictly complied with the ethical principles outlined in the Declaration of Helsinki. Prospective registration was completed at ClinicalTrials.gov (Identifier: NCT03162133; Registration Date: 12 May 2017). Written informed consent was obtained from all participants before commencement of the trial. As a pilot study, its primary objectives were to assess the feasibility of the 12-week Baduanjin intervention (including adherence rates and safety) and explore preliminary efficacy signals to inform future large-scale trials.

Participants

Participant recruitment was systematically conducted at the breast surgery clinic of Guangdong General Hospital between November 2017 and April 2018. Inclusion criteria included: 1) age ranging from 18 to 75 years; 2) histologically confirmed stage I to III breast cancer diagnosed between 0.5 and 8 years prior to enrollment; 3) continuous aromatase inhibitor therapy for more than six months; 4) menopausal syndrome severity confirmed by a modified Kupperman Index score of 6 or higher [31]; and 5) no prior Baduanjin exercise practice within the preceding six months. Exclusion criteria encompassed: i) severe comorbidities (e.g., uncontrolled cardiovascular disease, severe osteoporosis) or planned surgical interventions during the study period; and ii) participation in high-intensity physical activities

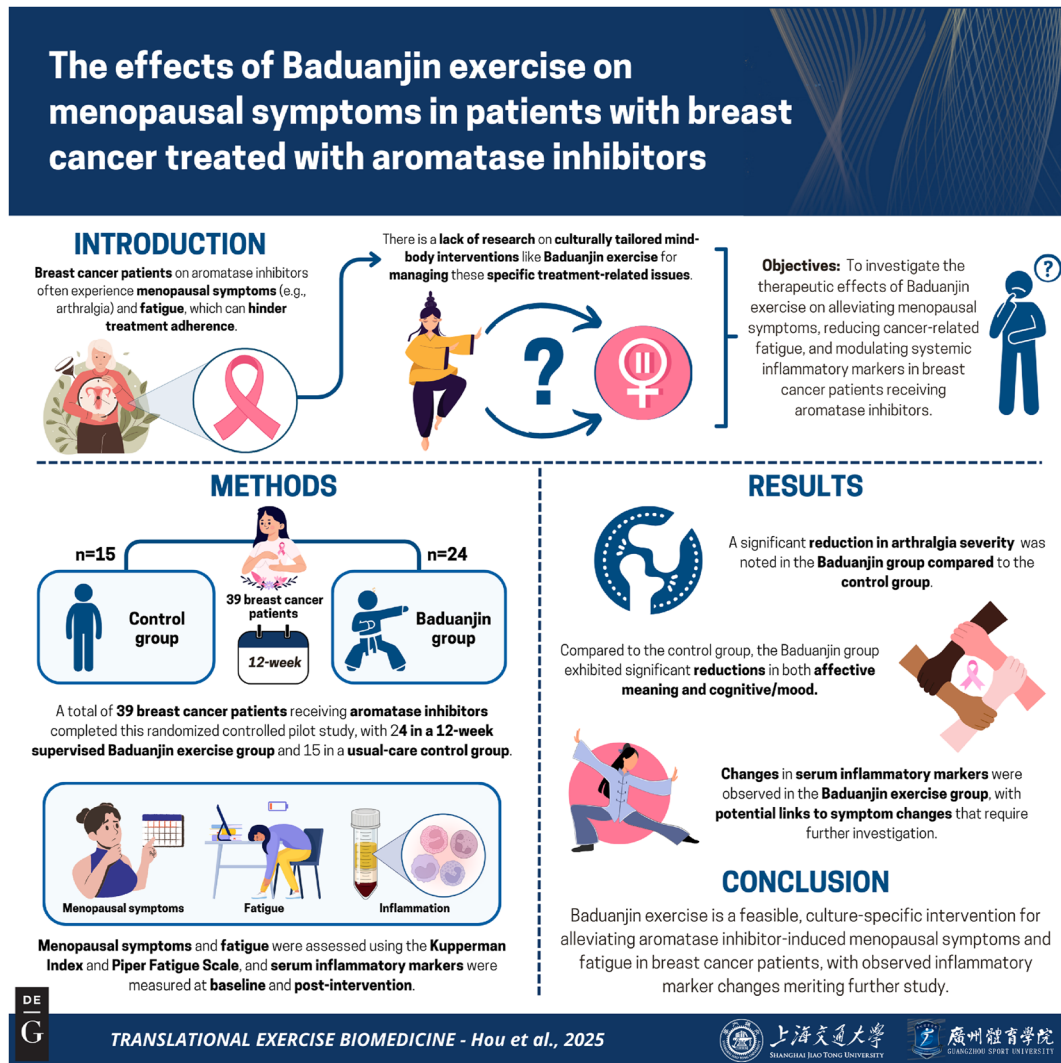


Figure 1: Graphical representation of this study. Key points: (1) breast cancer patients on aromatase inhibitors often experience menopausal symptoms (e.g., arthralgia) and cancer-related fatigue, which hinder treatment adherence, while culturally tailored mind-body interventions like Baduanjin are under-researched for these issues. (2) a randomized pilot study enrolled 39 breast cancer patients on aromatase inhibitors, with 24 in a 12-week supervised Baduanjin exercise group and 15 in control group, assessing symptoms via the Kupperman index/piper fatigue scale and serum inflammatory markers. (3) the Baduanjin group showed reduced arthralgia severity, improved fatigue dimensions, and altered serum inflammatory markers, supporting its feasibility as a culture-specific intervention with further investigation needed on inflammation-symptom links. Figure created with BioRender.

exceeding 5 h per week. Diagnostic verification was performed through comprehensive medical record review. Baseline assessments were systematically collected to characterize participants, including: 1) demographic characteristics (age, marital status, employment status); 2) clinical profiles (breast cancer stage, time since initial diagnosis, duration of aromatase inhibitor therapy); 3) health status indicators (comorbidities, treatment-related complications); and 4) pre-interventional physical activity profiles. Participants were randomly assigned to the Baduanjin exercise or control group via a computer-generated simple randomization sequence (1:1 allocation) managed by an independent statistician not

involved in participant recruitment or outcome assessment. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes. Baseline characteristics and attrition rate are presented in Results (Table 1).

Study interventions

The intervention protocol for the Baduanjin exercise group consisted of a 12-week supervised regimen involving three structured sessions per week, each lasting 90 min. Each session was conducted in a group format at the Sports

Table 1: Baseline characteristics of patients.^a

Characteristics	Control group (n=35)	Exercise group (n=35)	p-Value ^b
Age, years	54.43 (8.68)	54.31 (7.24)	0.95
Marital status, no. (%)			
Married	29 (82.9)	25 (71.4)	0.25
Divorced/separated	1 (2.9)	0 (0)	
Single	1 (2.9)	3 (8.6)	
Unclear	4 (11.3)	7 (20)	
Employment status, no. (%)			
Employed full or part-time	17 (48.6)	13 (37.1)	0.32
Unemployed	3 (8.6)	3 (8.6)	
Retired	15 (42.8)	19 (54.3)	
Unclear	0 (0)	0 (0)	
Time since diagnosis, years	2.91 (1.7)	3.17 (2.64)	0.63
Time since initiating AI, years	2.42 (1.85)	2.77 (2.37)	0.50
Overall stage, no. (%)			
I	6 (17.1)	7 (20)	0.57
II	20 (57.1)	21 (60)	
III	9 (25.8)	7 (20)	
Missing/NA	0 (0)	0 (0)	
Attrition	20 (57.1)	11 (31.4)	0.32

SD, standard deviation; AI, aromatase inhibitors. ^aData are presented as the mean (SD) for continuous variables and frequency (percentage) for categorical variables. ^bp-Value for difference between groups.

Medicine and Rehabilitation Center of Guangzhou Sport University, with on-site supervision by certified coaches to ensure the accuracy of movements. Each session was systematically divided into three phases: a 10-min preparatory warm-up, a 70-min standardized Baduanjin exercise regimen (comprising eight foundational postures executed eight times per session), and a 10-min cooldown period. Movement execution was synchronized with diaphragmatic breathing techniques (inhalation during postural extension phases, exhalation during relaxation phases). Instruction was provided by certified Qigong instructors with a minimum of five years of professional experience, adhering strictly to the 2017 National Fitness Qigong Baduanjin Standardized Guidelines [32]. The control cohort received routine clinical care without additional exercise interventions. Regarding blinding procedures, while it was not feasible to blind participants or Baduanjin instructors to the group allocation due to the physical nature of the intervention, blinding was rigorously implemented for both scale assessments (e.g., Kupperman Index, Piper Fatigue Scale) and blood sample analysis. Trained research assistants conducting scale evaluations and laboratory technicians responsible for cytokine detection (TNF- α , IL-6, IL-1 β) were

kept unaware of participant grouping to prevent subjective bias. Additionally, an independent statistician uninvolved in data collection performed all analyses using de-identified data, and all assessors underwent standardized training to ensure consistent operational procedures. These measures were collectively implemented to minimize potential measurement bias.

Outcome measurements

Menopausal symptom severity was quantified through standardized instruments (Kupperman Index and Piper Fatigue Scale) during baseline and post-intervention (48 h after the final exercise session) to avoid acute exercise-induced fluctuations in cytokines.

The Kupperman index

The modified Kupperman index, validated for evaluating menopausal symptoms in Chinese breast cancer survivors [31], comprises a cumulative score derived from 11 symptom-specific subscales: hot flashes, paresthesia, insomnia, nervousness, melancholia, vertigo, fatigue, joint and muscle pain, headaches, palpitations, and formication. Each subscale employs a scoring range from 0 to 3, where 0 indicates absence of symptoms, 1 represents mild symptoms, 2 corresponds to moderate symptoms, and 3 denotes severe symptoms. The total score is calculated by applying differential weighting coefficients: hot flashes are assigned a fourfold weighting, paresthesia, insomnia, and nervousness receive double weighting, while all remaining symptoms are assigned single weighting. This calculation method yields a maximum possible total score of 45.

The piper fatigue scale

Fatigue severity was quantified using the validated revised Piper Fatigue Scale [33], a widely used tool with established reliability in cancer populations [30, 34] which comprises 22 items systematically structured across four clinically recognized fatigue dimensions: behavioral manifestation/severity, affective interpretation, sensory perception, and cognitive-emotional impact. Each item utilized an 11-point Likert scale (0=no fatigue; 10=extreme fatigue), with domain-specific composite scores calculated as arithmetic means of constituent items. The global fatigue index was subsequently derived from averaging these four domain scores, providing a comprehensive fatigue assessment metric.

Serum inflammatory biomarkers assay

Fasting venous blood samples were collected under standardized morning conditions during both baseline and post-intervention phases (minimum 48-h interval after the final session). Serum separation was performed through centrifugation at 5,000 revolutions per minute for 10 min under controlled temperature conditions (4 °C). Quantitative measurement of interleukin-1 β (IL-1 β ; R&D Systems catalog DLB50), interleukin-6 (IL-6; catalog D6050B), and tumor necrosis factor- α (TNF- α ; catalog DTA00D) was conducted using validated enzyme-linked immunosorbent assay kits (R&D Systems, Minneapolis, MN, USA) according to established protocols. All samples underwent duplicate testing with averaged results to ensure analytical precision, while laboratory analysts remained blinded to group assignments.

Statistical analysis

Statistical analyses were performed using SPSS Statistics version 25.0 (IBM Corp., Armonk, NY). Prior to analyses, normality of continuous variables was verified using the Shapiro–Wilk test, with all outcome measures meeting normality criteria ($p > 0.05$). Baseline characteristics were presented as mean with standard deviation (SD) for continuous variables and frequency (percentage) for categorical measures. Intergroup comparisons of continuous parameters were analyzed via independent two-sample t -tests, whereas categorical variables were examined using Pearson's chi-square tests. Longitudinal outcome measures were expressed as mean $\pm$ SD. Between-group differences across timepoints (baseline vs. post-intervention) were evaluated through independent t -tests, while within-group temporal changes were assessed using paired-sample t -tests. Statistical significance was defined as two-tailed p values < 0.05 . Given the pilot nature of this study, no correction for multiple comparisons was applied to prioritize detection of preliminary efficacy signals, with results interpreted cautiously.

Results

Subject baseline characteristics

The participants flow through all stages of the study is comprehensively depicted in Figure 2. Of the 70 participants initially enrolled and randomized, a total of 39 individuals (55.7 %) successfully completed the full 12 – week intervention protocol. The attrition rate was 31.4 % (11 out of 35

participants) in the Baduanjin exercise group and 57.1 % (20 out of 35 participants) in the control group. Statistical analysis revealed no significant difference in attrition rates between the two groups. For the control group, which began with 35 randomized participants, 9 participants were lost to follow-up due to a lack of sustained interest in the study procedures. Additionally, 11 participants chose to discontinue the intervention prematurely. As a result, 15 participants in the control group completed all aspects of the study. In the Baduanjin exercise group, starting with an equal initial cohort of 35 randomized participants, 3 participants were lost to follow-up because of diminished interest, and 8 participants discontinued the intervention. Ultimately, 24 participants in the Baduanjin group fulfilled the entire study protocol. Demographic and clinical characteristics of the included patients at baseline are presented in Table 1, revealing no statistically significant intergroup differences in baseline parameters including age distribution, marital status, employment status, disease duration (range: 0.5–8 years post-diagnosis), duration of aromatase inhibitor therapy, or tumor staging classification.

The figure depicts the participant flow throughout the study. Initially, 82 individuals were enrolled and screened for eligibility. Among them, 10 were excluded: 2 had prior Baduanjin training experience, 5 declined participation, and 3 met cancer-related exclusion criteria. The remaining 72 participants underwent pre-intervention evaluation, with 2 further excluded (1 due to ineligibility per medical records, 1 with mobility/functional limitations). A total of 70 participants were then randomized: 35 to the control group (maintaining their usual lifestyle without Baduanjin intervention) and 35 to the Baduanjin group (receiving the allocated intervention). During follow-up, 9 control participants were lost to follow-up (due to disinterest) and 11 discontinued the intervention; in the Baduanjin group, 3 were lost to follow-up (disinterest) and 8 discontinued the intervention. Finally, 15 participants from the control group and 24 from the Baduanjin group were included in the analysis.

Effects of Baduanjin exercise on the Kupperman index

Table 2 presents the longitudinal changes in Kupperman Index scores following the 12-week intervention. Baseline assessments demonstrated comparable scores between the Baduanjin exercise and control groups for all individual symptom domains and total composite scores. Post-intervention assessment revealed no significant between-group differences in total Kupperman Index scores. However, the Baduanjin exercise group exhibited a statistically

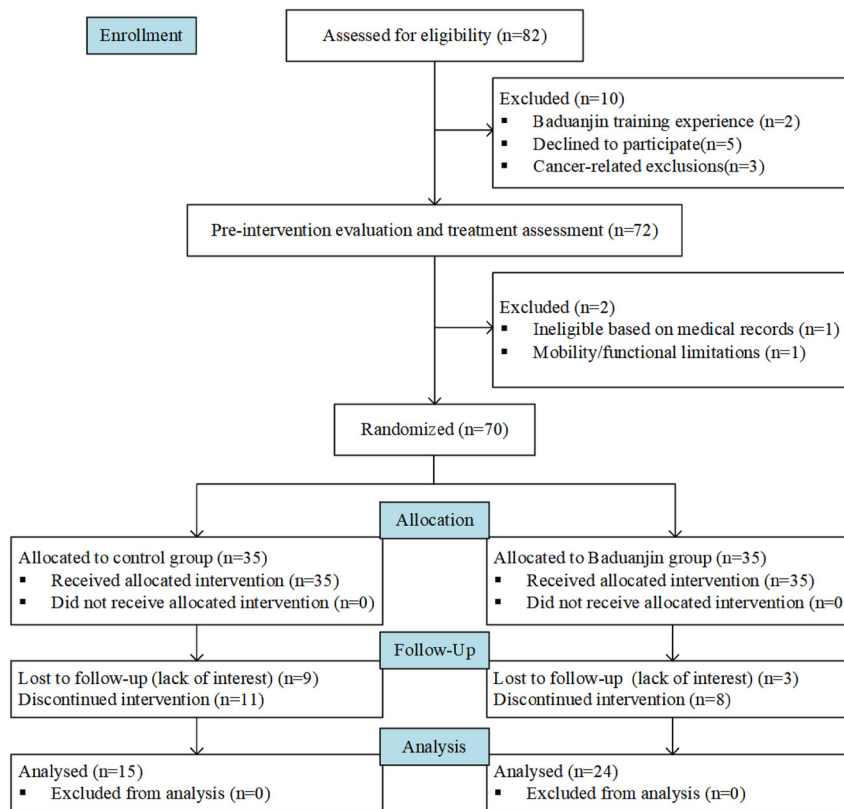


Figure 2: Flow diagram showing participant enrollment and grouping.

significant reduction in arthralgia severity compared to controls ($p < 0.05$). A clinically observable decrease in hot flash frequency was also documented in the Baduanjin exercise group, though this difference did not achieve statistical significance ($p = 0.059$).

Effects of Baduanjin exercise on the piper fatigue scale

Table 3 details the shifts in fatigue levels as indicated by the Piper Fatigue Scale. At the outset, equivalence was noted between the groups. Post-intervention, however, the Baduanjin exercise group exhibited a notably reduced level of affective meaning compared to the control group, achieving statistical significance ($p < 0.05$). In comparing the control group, the Baduanjin exercise group showed significant decreases of both affective meaning and cognitive/mood ($p < 0.05$).

Effects of Baduanjin exercise on serum inflammatory biomarkers

Table 4 presents the longitudinal changes in serum inflammatory biomarkers. Baseline and post-intervention comparisons showed no statistically significant between-

group differences in IL-6 concentrations. However, the Baduanjin exercise group demonstrated a significant elevation in IL-6 levels compared to the control group when analyzing within-group changes across the intervention period ($p < 0.05$).

Discussion

Contemporary advancements in oncological diagnostics and therapeutics have significantly enhanced prognostic outcomes for breast cancer [35]. However, treatment-induced complications – particularly among patients undergoing aromatase inhibitor therapy – persistently compromise quality-adjusted life years through menopausal symptom burden and cancer-related fatigue [36, 37]. This randomized controlled pilot study provides novel evidence that a 12-week Baduanjin exercise intervention protocol effectively attenuates menopausal symptomatology (particularly arthralgia severity) and mitigates multidimensional fatigue parameters in this clinical population. Mechanistically, the observed IL-6 modulation suggests potential anti-inflammatory pathways underlying these therapeutic effects, though further investigation is required to elucidate precise biological mechanisms.

Table 2: Effects of Baduanjin exercise on the Kupperman index.^a

	Baseline		p-Value ^b	Post-intervention		p-Value ^b	Change		p-Value ^c
	Control	Exercise		Control	Exercise		Control	Exercise	
Hot flashes	0.73 ± 0.59	0.96 ± 0.91	0.400	1.33 ± 0.62	1.08 ± 0.77	0.298	0.60 ± 0.63	0.13 ± 0.80	0.059
Paresthesia	1.00 ± 0.92	1.04 ± 0.62	0.867	1.00 ± 0.85	0.79 ± 0.66	0.394	0.00 ± 0.93	-0.25 ± 0.79	0.375
Insomnia	0.93 ± 0.70	1.00 ± 0.72	0.779	0.93 ± 0.70	0.96 ± 0.75	0.918	0.00 ± 0.53	-0.04 ± 0.91	0.873
Nervousness	0.87 ± 0.52	0.92 ± 0.58	0.787	0.67 ± 0.61	0.67 ± 0.64	0.657	-0.20 ± 0.77	-0.17 ± 0.70	0.890
Melancholia	0.47 ± 0.64	0.79 ± 0.83	0.205	0.60 ± 0.63	0.50 ± 0.66	0.643	0.13 ± 0.52	-0.29 ± 0.95	0.122
Vertigo	0.80 ± 0.56	0.88 ± 0.80	0.752	0.67 ± 0.64	0.60 ± 0.63	1.000	-0.13 ± 0.74	-0.21 ± 0.88	0.786
Fatigue	1.13 ± 0.35	1.13 ± 0.67	0.965	1.07 ± 0.45	0.96 ± 0.36	0.415	-0.07 ± 0.26	-0.17 ± 0.82	0.649
Arthralgia and myalgia	1.87 ± 0.64	1.96 ± 0.69	0.681	1.80 ± 0.68	1.33 ± 0.48	0.467	-0.07 ± 0.59	-0.62 ± 0.82	0.029 [§]
Headache	0.67 ± 0.48	0.67 ± 0.70	1.000	0.87 ± 0.74	0.63 ± 0.58	0.262	0.20 ± 0.68	-0.04 ± 0.62	0.262
Palpitations	0.93 ± 0.88	0.58 ± 0.77	0.183	0.53 ± 0.74	0.46 ± 0.66	0.744	-0.40 ± 0.83	-0.13 ± 0.54	0.215
Formication	0.47 ± 0.52	0.46 ± 0.51	0.961	0.40 ± 0.51	0.42 ± 0.65	0.933	-0.07 ± 0.46	-0.04 ± 0.69	0.902
Total score	14.9 ± 5.64	16.2 ± 6.26	0.504	16.47 ± 5.08	14.29 ± 6.58	0.282	1.60 ± 3.68	-1.92 ± 6.99	0.081

SD, standard deviation. ^aData were presented as mean ± SD; control group (n=15); exercise group (n=24). p-Value^b for difference between groups at baseline or post-intervention. p-Value^c for change between groups from baseline to post-intervention.

Table 3: Effects of Baduanjin exercise on the piper fatigue scale.^a

	Baseline		p-Value ^b	Post-intervention		p-Value ^b	Change		p-Value ^c
	Control	Exercise		Control	Exercise		Control	Exercise	
Behavioral/severity	2.79 ± 2.37	3.07 ± 2.41	0.727	2.86 ± 2.31	2.25 ± 1.89	0.378	0.07 ± 0.81	-0.82 ± 1.84	0.088
Affective meaning	1.97 ± 1.83	3.00 ± 2.55	0.181	3.02 ± 2.51	1.75 ± 1.27	0.043	1.06 ± 1.83	-1.24 ± 2.45	0.003
Sensory	4.29 ± 2.31	4.23 ± 2.46	0.934	4.15 ± 2.02	3.49 ± 1.52	0.255	-0.15 ± 2.61	-0.74 ± 2.19	0.453
Cognitive/mood	3.16 ± 1.88	4.01 ± 2.66	0.283	3.88 ± 2.12	3.24 ± 1.49	0.275	0.72 ± 1.34	-0.78 ± 2.15	0.021
Total score	3.04 ± 0.1.79	3.57 ± 2.27	0.448	3.47 ± 1.74	2.69 ± 1.34	0.124	0.42 ± 0.74	-0.89 ± 1.75	0.009

PFS, piper fatigue scale; SD, standard deviation. ^aData were presented as mean ± SD; control group (n=15); exercise group (n=24). p-Value^b for difference between groups at baseline or post-intervention. p-Value^c for change between groups from baseline to post-intervention.

Table 4: Effects of Baduanjin exercise on serum inflammatory biomarkers.^a

	Baseline		p-Value ^b	Post-intervention		p-Value ^b	Change		p-Value ^c
	Control	Exercise		Control	Exercise		Control	Exercise	
IL-1β, pg/mL	67.41 ± 15.34	66.34 ± 15.82	0.835	80.49 ± 22.67	66.89 ± 15.27	0.031	13.07 ± 25.71	0.56 ± 16.64	0.072
IL-6, pg/mL	3.54 ± 0.42	3.60 ± 0.56	0.717	4.56 ± 0.72	6.15 ± 1.29	0.000	1.02 ± 0.47	2.54 ± 1.25	0.000
TNF-α, pg/mL	49.00 ± 9.46	47.53 ± 6.94	0.577	56.35 ± 6.57	49.80 ± 7.44	0.008	7.34 ± 10.60	2.27 ± 5.79	0.061

IL-1β, interleukin-1β; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; SD, standard deviation. ^aData were presented as mean ± SD; control group (n=15); exercise group (n=24). p-Value^b for difference between groups at baseline or post-intervention. p-Value^c for change between groups from baseline to post-intervention.

Baduanjin exercise, a multimodal mind-body practice rooted in traditional Chinese medicine, combines physical postures with cognitive engagement and regulated breathing techniques, demonstrating therapeutic benefits for chronic conditions in female breast cancer patients [38]. This low-complexity intervention, comprising eight biomechanically optimized movements derived from historical wellness traditions, exhibits high accessibility across diverse demographics [17]. The efficacy of Baduanjin for improving

psychosocial well-being in breast cancer patients is supported by accumulating evidence from systematic reviews and meta-analyses. These analyses have consistently confirmed its benefits in enhancing health-related quality of life and alleviating depressive symptoms [12–14, 32, 39]. The present findings provide supportive evidence regarding the potential of Baduanjin exercise in ameliorating vasomotor disturbances, with particular reference to reductions in hot flash frequency observed in aromatase inhibitor-treated

patient cohorts [40]. These outcomes appear congruent with established clinical recommendations advocating mind-body interventions as therapeutic strategies for addressing treatment-induced menopausal symptoms [41]. Notably, we observed clinically meaningful reductions in arthralgia severity – a prevalent complication affecting distal joints that frequently compromises treatment adherence [42]. While previous meta-analyses report limited analgesic effects of Baduanjin exercise [13], our results suggest outcome variability may stem from differences in pain etiology (e.g., postoperative vs. treatment-induced), intervention protocols, and population-specific adaptations, underscoring the need for phenotype-stratified investigations.

Breast cancer survivors undergoing aromatase inhibitor therapy frequently report elevated fatigue severity concomitant with menopausal symptomatology. The fundamental mechanism behind fatigue is often linked to inflammation, a response typically triggered by standard cancer therapies, including chemotherapy, or by the cancer itself [43]. Our findings demonstrate Baduanjin exercise's efficacy in attenuating multidimensional fatigue manifestations, particularly affective and cognitive/mood dimensions, corroborating existing evidence of its therapeutic potential against cancer-related fatigue [39]. Contemporary randomized controlled trial data substantiate these anti-fatigue effects across heterogeneous patient populations, though reduced effect consistency is noted in cohorts aged over 55 years [15]. Mechanistic investigations implicate aromatase inhibitors as potential contributors to fatigue pathophysiology through inflammatory pathways [44, 45], with circulating biomarkers like IL-6 exhibiting dual regulatory properties in inflammatory cascades [46]. IL-6 exhibits context-dependent dual roles in cancer, acting as either a suppressor or promoter of tumor development. During exercise, IL-6 is primarily released from skeletal muscles, whereas in inflammatory foci or the tumor microenvironment, it is secreted by leukocytes and stromal cells. Muscle-derived IL-6 exerts protective effects by enhancing insulin sensitivity in glycogen-storing tissues, stimulating anti-inflammatory cytokine production, mobilizing cytotoxic immune cells, and reducing DNA damage in cancer cells – biological actions that may inhibit cancer initiation and progression. Conversely, sustained IL-6 signaling within inflamed or tumor microenvironments drives chronic low-grade inflammation and activates pro-tumorigenic pathways, thereby promoting cancer advancement [29]. Additionally, IL-6 has been implicated as a critical mediator of pathological pain, including bone cancer pain, through mechanisms such as nociceptor sensitization and amplification of inflammatory signaling cascades [47].

Discrepancies between our findings and other Baduanjin studies likely stem from population-specific differences.

For example, middle-aged women demonstrated reduced IL-6 after 12-week Baduanjin, likely reflecting systemic anti-inflammatory effects in metabolically intact populations [48]. Post-stroke patients with depression similarly exhibited decreased IL-6 following combined Baduanjin and psychotherapy, potentially via neuroendocrine-immune regulation of stress-driven inflammation [49]. Conversely, cognitively frail older adults showed non-significant IL-6 changes post-24-week Baduanjin practice, possibly due to age-related immunosenescence or baseline inflammatory lability [50]. Our cohort's distinct characteristics – breast cancer survivors receiving aromatase inhibitors – introduce critical variables: these agents may disrupt muscle metabolic equilibrium, potentially augmenting myokine IL-6 secretion during rhythmic motor activity [42, 51]. This muscle-derived IL-6 could represent a transient adaptive response promoting glucose homeostasis and anti-inflammatory cytokine synthesis [29], distinguishable from pathogenic IL-6 signaling within tumor microenvironments. The observed elevation might therefore indicate beneficial “metabolic-inflammatory” uncoupling, wherein exercise-induced myokines mitigate therapy-related metabolic disturbances without potentiating pro-tumorigenic cascades. Notably, our observed IL-6 elevation post-Baduanjin exercise contrasts with conventional exercise-induced anti-inflammatory responses [30], suggesting modality-specific immunomodulatory mechanisms requiring further elucidation.

This study provides novel insights into Baduanjin exercise's therapeutic effects on aromatase inhibitor-associated menopausal symptoms in breast cancer patients, while acknowledging methodological constraints. A key limitation is the small completed sample size (total $n=39$), which limits the feasibility of sensitivity analyses; multiple imputation or subgroup analyses in such small samples may introduce bias, so additional sensitivity tests were not performed [52]. This underscores the necessity for future studies with expanded sample sizes to verify the robustness of the findings. Other limitations include the notable attrition discrepancy (57.1 % in the control group vs. 31.4 % in the Baduanjin exercise group, $p=0.03$) – likely due to the lack of structured supervision in the control group – potentially biasing results toward participants with milder symptoms or higher adherence in the control cohort. From a patient management perspective, these findings highlight the importance of personalized support to enhance adherence: clinicians should proactively identify patients at risk of attrition (e.g., those showing early signs of disinterest or perceived burden), use regular follow-ups and tailored motivational counseling to improve retention, and integrate peer-support systems (where experienced participants share their journeys) to boost patients' confidence and

commitment to interventions like Baduanjin. Additionally, the heterogeneous age range (36–70 years), absence of neurocognitive assessments, and 12-week intervention duration (insufficient to address chronic inflammation from prolonged aromatase inhibitor use) further restrict the generalizability of conclusions. In summary, this pilot study suggests that Baduanjin exercise may serve as a feasible, low-intensity adjunctive therapy for ameliorating aromatase inhibitor-induced menopausal symptoms and fatigue, with distinct immunomodulatory effects on IL-6. Further research with larger samples, extended interventions, comprehensive mechanistic assessments (including exploration of IL-6's dual roles), and refined methodologies (e.g., standardized retention strategies and age-stratified analyses) is needed to validate these findings and clarify the underlying mechanisms.

Conclusions

This pilot study provides preliminary evidence that 12-week Baduanjin exercise may alleviate specific aromatase inhibitor-induced menopausal symptoms (notably arthralgia) and reduce multidimensional fatigue in breast cancer patients, with concurrent modulation of inflammatory markers such as IL-6, tentatively supporting its potential as a low-intensity complementary intervention for managing treatment-related complications; however, due to limitations including a small sample size ($n=39$), notable attrition bias, and short intervention duration, these findings should be interpreted cautiously, and further well-powered trials with larger cohorts, extended follow-up, and mechanistic assessments – particularly regarding IL-6's context-dependent role – are needed to validate its therapeutic value.

Research ethics: This study was performed under the rules of the Declaration of Helsinki, approved by the Ethics Committee of Guangdong General Hospital (GDREC2016424H (R1)).

Informed consent: Informed consent was obtained from all individuals included in this study, or their legal guardians or wards.

Author contributions: Jingwen Liao and Hao Lan analyzed the data, drew the graph, and drafted the tables and manuscript. Hao Lan conceived and designed the research, performed the research, analyzed the data, contributed to materials and analysis tools. Kun Wang provided clinical diagnosis information and other support for patients. Li Cai performed the research and conducted the Baduanjin exercise program. Min Hu and Xiaohui Hou designed the research, provided assistance, and reviewed the manuscript

and tables. The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Use of Large Language Models, AI and Machine Learning

Tools: We used the AI tool DeepSeek to assist with language polishing and improving the readability of the initial manuscript draft. All AI-generated content was thoroughly reviewed, revised, and approved by the authors, who take full responsibility for the entire content of the published work.

Conflict of interest: The authors declare no conflict of interest. Min Hu serves as an Editor-in-Chief for Translational Exercise Biomedicine, but was not involved in the handling, editorial review, or decision-making process for this manuscript. Xiaohui Hou serves as an In-house Managing-editor for Translational Exercise Biomedicine, but was not involved in the handling, editorial review, or decision-making process for this manuscript.

Research funding: This work was supported by the Guangdong Provincial Key Laboratory of Physical Activity and Health Promotion [grant numbers: 2021B1212040014] and the Guangdong Provincial Key Laboratory of Human Sports Performance Science [grant numbers: 2024B1212020009].

Data availability: The raw data can be obtained on request from the corresponding author.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024;74:229–63.
2. Xiong X, Zheng LW, Ding Y, Chen YF, Cai YW, Wang LP, et al. Breast cancer: pathogenesis and treatments. *Signal Transduct Targeted Ther* 2025;10:49.
3. De La Cruz L, Blankenship SA, Chatterjee A, Geha R, Nocera N, Czerniecki BJ, et al. Outcomes after oncoplastic breast-conserving surgery in breast cancer patients: a systematic literature review. *Ann Surg Oncol* 2016;23:3247–58.
4. Kohler BA, Sherman RL, Howlader N, Jemal A, Ryerson AB, Henry KA, et al. Annual report to the nation on the status of cancer, 1975–2011, featuring incidence of breast cancer subtypes by race/ethnicity, poverty, and state. *J Natl Cancer Inst* 2015;107:djv048.
5. Papakonstantinou A, Villacampa G, Navarro V, Oliveira M, Valachis A, Pascual T, et al. Adjuvant endocrine treatment strategies for non-metastatic breast cancer: a network meta-analysis. *eClinicalMedicine* 2025;81:103116.
6. Gradishar WJ, Moran MS, Abraham J, Aft R, Agnese D, Allison KH, et al. NCCN Guidelines(R) insights: Breast cancer, Version 4.2021. *J Natl Compr Cancer Netw* 2021;19:484–93.
7. Runowicz CD, Leach CR, Henry NL, Henry KS, Mackey HT, Cowens-Alvarado RL, et al. American cancer society/American society of clinical oncology breast cancer survivorship care guideline. *CA Cancer J Clin* 2016;66:43–73.

8. Banning M. Adherence to adjuvant therapy in post-menopausal breast cancer patients: a review. *Eur J Cancer Care (Engl)* 2012; 21:10–9.
9. Kyvernitis I, Ziller V, Hars O, Bauer M, Kalder M, Hadji P. Prevalence of menopausal symptoms and their influence on adherence in women with breast cancer. *Climacteric* 2014;17:252–9.
10. Peterson LL, Ligibel JA. Physical activity and breast cancer: an opportunity to improve outcomes. *Curr Oncol Rep* 2018;20:50.
11. Bender CM, Sereika SM, Gentry AL, Zhu Y, Wagner M, Cuglewski C, et al. Aerobic exercise and aromatase inhibitor-associated musculoskeletal symptoms: results of a randomized clinical trial. *Support Care Cancer* 2025;33:244.
12. Gong X, Rong G, Wang Z, Zhang A, Li X, Wang L. Baduanjin exercise for patients with breast cancer: a systematic review and meta-analysis. *Compl Ther Med* 2022;71:102886.
13. Ye XX, Ren ZY, Vafaei S, Zhang JM, Song Y, Wang YX, et al. Effectiveness of baduanjin exercise on quality of life and psychological health in postoperative patients with breast cancer: a systematic review and meta-analysis. *Integr Cancer Ther* 2022;21:15347354221104092. <https://doi.org/10.1177/15347354221104092>.
14. Chen Y, Zuo X, Tang Y, Zhou Z. The effects of Tai chi and Baduanjin on breast cancer patients: systematic review and meta-analysis of randomized controlled trials. *Front Oncol* 2024;14:1434087.
15. Liu H, Liu S, Xiong L, Luo B. Efficacy of Baduanjin for treatment of fatigue: a systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltim)* 2023;102:e34707.
16. Zou L, Sasaki JE, Wang H, Xiao Z, Fang Q, Zhang M. A systematic review and meta-analysis baduanjin qigong for health benefits: randomized controlled trials. *Evid Based Complement Alternat Med* 2017;2017: 4548706.
17. Koh TC. Baduanjin – an ancient Chinese exercise. *Am J Chin Med* 1982; 10:14–21.
18. Cocks K, Wells JR, Johnson C, Schmidt H, Koller M, Oerlemans S, et al. Content validity of the EORTC quality of life questionnaire QLQ-C30 for use in cancer. *Eur J Cancer* 2023;178:128–38.
19. Musoro JZ, Coens C, Sprangers MAG, Brandberg Y, Groenvold M, Flechtner HH, et al. Minimally important differences for interpreting EORTC QLQ-C30 change scores over time: a synthesis across 21 clinical trials involving nine different cancer types. *Eur J Cancer* 2023;188: 171–82.
20. Hiensch AE, Depenbusch J, Schmidt ME, Monninkhof EM, Pelaez M, Clauss D, et al. Supervised, structured and individualized exercise in metastatic breast cancer: a randomized controlled trial. *Nat Med* 2024; 30:2957–66.
21. Fallowfield LJ, Leaity SK, Howell A, Benson S, Cella D. Assessment of quality of life in women undergoing hormonal therapy for breast cancer: validation of an endocrine symptom subscale for the FACT-B. *Breast Cancer Res Treat* 1999;55:189–99.
22. Tolaney SM, Guarneri V, Seo JH, Cruz J, Abreu MH, Takahashi M, et al. Long-term patient-reported outcomes from monarchE: abemaciclib plus endocrine therapy as adjuvant therapy for HR+, HER2-node-positive, high-risk, early breast cancer. *Eur J Cancer* 2024;199: 113555.
23. Lustberg M, Fan-Havard P, Wong FL, Hill K, Phelps MA, Herrera KW, et al. Randomized placebo-controlled, double-blind clinical trial of nanoemulsion curcumin in women with aromatase inhibitor-induced arthropathy: an Alliance/NCORP pilot trial. *Breast Cancer Res Treat* 2024;205:61–73.
24. Chie WC, Chang KJ, Huang CS, Kuo WH. Quality of life of breast cancer patients in Taiwan: validation of the Taiwan Chinese version of the EORTC QLQ-C30 and EORTC QLQ-BR23. *Psychooncology* 2003;12: 729–35.
25. Paramanandam VS, Dylke E, Clark GM, Daptardar AA, Kulkarni AM, Nair NS, et al. Prophylactic use of compression sleeves reduces the incidence of arm swelling in women at high risk of breast cancer-related lymphedema: a randomized controlled trial. *J Clin Oncol* 2022; 40:2004–12.
26. Dent R, Cortés J, Pusztai L, McArthur H, Kümmel S, Bergh J, et al. Neoadjuvant pembrolizumab plus chemotherapy/adjuvant pembrolizumab for early-stage triple-negative breast cancer: Quality-of-Life results from the randomized KEYNOTE-522 study. *J Natl Cancer Inst* 2024;116:1654–63.
27. Wu S, Shi Y, Zhao Q, Men K. The relationship between physical activity and the severity of menopausal symptoms: a cross-sectional study. *BMC Womens Health* 2023;23:212.
28. Kim MJ, Cho J, Ahn Y, Yim G, Park HY. Association between physical activity and menopausal symptoms in perimenopausal women. *BMC Womens Health* 2014;14:122.
29. Orange ST, Leslie J, Ross M, Mann DA, Wackerhage H. The exercise IL-6 enigma in cancer. *Trends Endocrinol Metabol* 2023;34:749–63.
30. Hiensch AE, Mijwel S, Bargiela D, Wengström Y, May AM, Rundqvist H. Inflammation mediates exercise effects on fatigue in patients with breast cancer. *Med Sci Sports Exerc* 2021;53:496–504.
31. Tao M, Shao H, Li C, Teng Y. Correlation between the modified Kupperman index and the menopause rating scale in Chinese women. *Patient Prefer Adherence* 2013;7:223–9.
32. Liao J, Chen Y, Cai L, Wang K, Wu S, Wu L, et al. Baduanjin's impact on quality of life and sleep quality in breast cancer survivors receiving aromatase inhibitor therapy: a randomized controlled trial. *Front Oncol* 2022;12:807531.
33. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM, editors. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *Oncol Nurs Forum* 1998;25:677–84.
34. Hsiao CP, Wang D, Kaushal A, Saligan L. Mitochondria-related gene expression changes are associated with fatigue in patients with nonmetastatic prostate cancer receiving external beam radiation therapy. *Cancer Nurs* 2013;36:189–97.
35. Burstein HJ, Lacchetti C, Anderson H, Buchholz TA, Davidson NE, Gelmon KA, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: ASCO clinical practice guideline focused update. *J Clin Oncol* 2019;37:423–38.
36. Khosrow-Khavar F, Filion KB, Bouganim N, Suissa S, Azoulay L. Aromatase inhibitors and the risk of cardiovascular outcomes in women with breast cancer: a population-based cohort study. *Circulation* 2020;141:549–59.
37. Henry NL, Azzouz F, Desta Z, Li L, Nguyen AT, Lemler S, et al. Predictors of aromatase inhibitor discontinuation as a result of treatment-emergent symptoms in early-stage breast cancer. *J Clin Oncol* 2012;30: 936–42.
38. Leung KW, Yang YJ, Hui SS, Woo J. Mind-body health benefits of traditional Chinese qigong on women: a systematic review of randomized controlled trials. *Evid Based Complement Alternat Med* 2021;2021:7443498.
39. Kuo CC, Wang CC, Chang WL, Liao TC, Chen PE, Tung TH. Clinical effects of baduanjin qigong exercise on cancer patients: a systematic review and meta-analysis on randomized controlled trials. *Evid Based Complement Alternat Med* 2021;2021:6651238.
40. Chlebowski RT, Mortimer JE, Crandall CJ, Pan K, Manson JE, Nelson R, et al. Persistent vasomotor symptoms and breast cancer in the Women's health initiative. *Menopause* 2018;26:578–87.

41. Liu J, Nie G, Li Y, Wen Z, Lu L, Xie L, et al. Nonhormonal hot flash management for breast cancer survivors: a systematic review and network meta-analysis. *Evid Based Complement Alternat Med* 2020; 2020:4243175.
42. Hyder T, Marino CC, Ahmad S, Nasrazadani A, Brufsky AM. Aromatase inhibitor-associated musculoskeletal syndrome: understanding mechanisms and management. *Front Endocrinol* 2021;12:713700.
43. Bower JE, Lamkin DM. Inflammation and cancer-related fatigue: mechanisms, contributing factors, and treatment implications. *Brain Behav Immun* 2013;30:S48–57.
44. Bauml J, Chen L, Chen J, Boyer J, Kalos M, Li SQ, et al. Arthralgia among women taking aromatase inhibitors: is there a shared inflammatory mechanism with co-morbid fatigue and insomnia? *Breast Cancer Res* 2015;17:89.
45. Mao JJ, Farrar JT, Bruner D, Zee J, Bowman M, Seluzicki C, et al. Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor-related arthralgia: a randomized trial. *Cancer* 2014;120:3744–51.
46. Fuster JJ, Walsh K. The good, the bad, and the ugly of interleukin-6 signaling. *EMBO J* 2014;33:1425–7.
47. Zhou YQ, Liu Z, Liu ZH, Chen SP, Li M, Shahveranov A, et al. Interleukin-6: an emerging regulator of pathological pain. *J Neuroinflammation* 2016;13:141.
48. Chen HH, Yeh ML, Lee FY. The effects of baduanjin qigong in the prevention of bone loss for middle-aged women. *Am J Chin Med* 2006; 34:741–7.
49. Liu Y, Chen C, Du H, Xue M, Zhu N. Impact of Baduanjin exercise combined with rational emotive behavior therapy on sleep and mood in patients with poststroke depression: a randomized controlled trial. *Medicine (Baltim)* 2024;103:e38180.
50. Ye Y, Wan M, Lin H, Xia R, He J, Qiu P, et al. Effects of Baduanjin exercise on cognitive frailty, oxidative stress, and chronic inflammation in older adults with cognitive frailty: a randomized controlled trial. *Front Public Health* 2024;12:1385542.
51. Gupta A, Henry NL, Loprinzi CL. Management of aromatase inhibitor-induced musculoskeletal symptoms. *JCO Oncol Pract* 2020;16:733–9.
52. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;338:b2393.