



Effectiveness of Pilates and circuit-based exercise in reducing arthralgia in women during hormone therapy for breast cancer: a randomized, controlled trial

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Abstract

Objective To investigate the effect of Pilates compared with circuit-based exercise in reducing arthralgia in women during hormone therapy for breast cancer.

Design Single-blind randomized controlled trial, parallel.

Setting University hospital of Brasilia and Brazilian Association for Assistance to People with Cancer.

Participants Sixty women with arthralgia were recruited. Eligibility criteria included women complaining of arthralgia during hormone therapy for breast cancer. The exclusion criteria were women with active cancer, lymphedema, limitations to physical exercise, or limitation to answer some questionnaires.

Main outcome measures Primary: Pain. Secondary: Function, flexibility, and sleep quality. Outcomes were assessed at baseline and the end of the intervention (8 weeks) by the same blinded evaluator.

Intervention Sixty participants were randomly assigned 20 to each of the three groups: Pilates, circuit-based exercise, and control groups. Exercise was performed twice per week for 75 min, over a period of 8 weeks. Participants in the control group were instructed to continue their usual activities. The Kolmogorov-Smirnov test was used to verify the normality of the outcomes. Intergroup differences were calculated using Kruskal-Wallis test with post hoc Mann Whitney U testing and the parametric data between the three groups with ANOVA of repeated measures with Bonferroni post hoc.

Results The Pilates group demonstrated a significant difference in pain reduction compared to the circuit group (mean difference: -1.95 points, $p = 0.020$).

Conclusion Pilates was more effective than circuit-based exercise in reducing arthralgia in women during hormone therapy for breast cancer.

Trial registration <http://www.ensaiosclinicos.gov.br/rg/RBR-3wsdhs/> Registered on Octob 16th 2017

Keywords Arthralgia · Endocrine therapy · Pilates · Circuit-based exercise

Introduction

Arthralgia, defined as pain or stiffness in the joints, is reported in 40–50% of women undergoing hormone therapy for breast cancer [1, 2]. Despite being a common condition [2], there is still no gold standard treatment for this. Reliable scientific evidence assessing treatments for arthralgia is lacking, with most studies having small samples, high risks of bias, and a lack of blinding [3]. In a recent meta-analysis [3] that addressed different types of arthralgia after hormone therapy, the authors highlighted the high risk of bias in clinical trials, and difficulty in finding appropriate guidelines recommending exercise for women with arthralgia during hormone therapy.

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Pilates and circuit-based exercise provide motivation and have the potential for adherence by women during breast cancer treatment [4]. A recent meta-analysis concluded that Pilates can be safely recommended for women with breast cancer [5]. Circuit-based exercise is defined by the Medical Subject Headings (MeSH) as “alternating sets of exercise that work out different muscle groups and that also alternate between aerobic and anaerobic exercises, which, when combined together, offer an overall program to improve strength, stamina, balance, or functioning” (available at www.ncbi.nlm.nih.gov/mesh/, 2015). Circuit-based exercise has been recently used in women with breast cancer and has been found to provide improved physical performance [6], making it a possible intervention for arthralgia. To date, no clinical trials have compared Pilates and circuit-based exercise for treating women with arthralgia.

The meta-analysis by Roberts et al. [3] assessed the types of interventions used to treat hormone therapy-induced morbidities. The authors highlighted the study by Irwin et al., who reported pain reduction in women with arthralgia [7] who combined aerobic exercise and strength training. The authors of the meta-analysis concluded that clinical trials with more rigorous controls are required to confirm the effectiveness of exercise for musculoskeletal dysfunctions induced by hormone therapy [3]. The purpose of this study was to compare Pilates against circuit-based exercise in reducing arthralgia in women treated with hormone therapy for breast cancer.

Methods

Participants

Sixty women complaining of arthralgia during hormone therapy for breast cancer were recruited via advertisements at university, posts on social media and at Brazilian Association for Assistance to People with Cancer between October 2017 and January 2018. Written informed consent was obtained from all participants, and the study was approved by the Local University Ethics Committee (number: 2.889.890).

The inclusion criteria were women complaining of arthralgia (one point in numerical rating scale (NRS) and one joint localized in brief pain inventory (BPI)) during hormone therapy for breast cancer. The exclusion criteria were women with active cancer, lymphedema, limitations to physical exercise, or limitation to answer some questionnaires [8, 9].

Study design

A single-blind (evaluator only) parallel randomized control trial (RCT) was designed to compare the effectiveness of Pilates and circuit-based exercise in reducing arthralgia in

women during hormone therapy for breast cancer. This RCT was designed according to the Consolidated Standards of Reporting Trials (CONSORT) checklist for RCTs and was registered (<http://www.ensaiosclinicos.gov.br/rg/RBR-3wsdhs/>).

Randomization, allocation, and blinding

A total of 60 participants were randomized with a 1:1 allocation for one of three groups: 20 for the Pilates group, 20 for the circuit-based exercise group, and 20 for the control group, using the website (<http://www.randomization.com>). Sealed opaque envelopes, sequentially numbered, were used to hide the allocation. An external administrator who was not involved in the recruitment or assessment of participants, to prevent selection bias, managed the random list. A second administrator not involved in data collection was assigned to open the envelopes with the random codes and deliver them to the participants to ensure concealed allocation. The assessments were performed by a third administrator, blinded to group allocation, that performed the evaluation for all outcomes before and after the intervention. Participants were instructed not to reveal to evaluator of which group they belonged to. Statistical analysis was performed by an external, blinded researcher.

Primary outcome measures

We assessed arthralgia via the numerical rating scale (NRS) [9], brief pain inventory (BPI) [10], and disabilities of the arm, shoulder, and hand (DASH) [11] at baseline (T0) and after 8 weeks of intervention (T8). The NRS was applied verbally, in which the participant provided pain intensity on a scale of 0–10, with 0 indicating “no pain” and 10 “worst pain imaginable” [9]. The participants’ joint pain intensity was evaluated at the time of intervention. The BPI was performed to localize joint pain. The DASH questionnaire was used to evaluate upper extremity function, with a final score between zero (no disability) and 100 (severe disability). This valid instrument had a high internal consistency (Cronbach’s: 0.91, intraclass correlation coefficient: 0.92) [11, 12].

Secondary outcome measures

Sociodemographic data, treatment details, use of pain medications, and information on comorbidities were collected through medical records and interviews with the participant. A physical evaluation was performed that measured body mass with a bioimpedance balance (OMRON Fat Analyzer, model HBF 514C) and height with a portable stadiometer (Personal Caprice Sanny). In addition, flexibility was measured using the sit and reach test (Wells Portable Sanny) [4], and quality of sleep was measured using the Pittsburgh Sleep

Quality Index (PSQI), with a score of > 5 indicating poor sleep quality and ≤ 5 indicating good sleep quality [13].

Procedures

Participants were evaluated at baseline (T0) and after 8 weeks (T8). The questionnaire of readiness for physical activity (PAR-Q) was administered at baseline. Adverse events and participant frequency were registered. Participants were monitored by telephone for adverse events and were instructed to report any event such as discomfort and worsening pain and were instructed not to change their usual activities, diet, or medications during the study.

The exclusions, losses, and the respective reasons are reported in the CONSORT diagram in Fig. 1.

Pilates and circuit-based exercise groups

The Pilates group performed seven basic exercises according to traditional mat Pilates methodology, and the circuit-based exercise group performed six exercises in stations (Table 1) [14–16]. The circuit and Pilates exercises were performed for 75 min each time.

Control group

Participants in the control group were instructed to maintain their usual activities (not to change their usual activities and diet during the study) throughout the intervention period and reevaluation. All participants had the opportunity to participate in Pilates or circuit after the study ended.

Statistical analyses

Sample size required to detect differences in primary pain outcome between the three study groups was calculated at the study design phase, considering a large effect size ($f = 0.40$), 80% power, and significance level of 5%. This calculation indicated the need for 60 participants (20 participants for each group).

Baseline characteristics were reported using absolute frequency and percentage measures for categorical variables, mean and standard deviation measures for continuous variables with normal distributions, and median and interquartile measures (25–75% percentiles) for continuous variables with non-normal distribution, with a 95% confidence interval. The Kolmogorov-Smirnov test was used to verify the normality of the outcomes. Sociodemographic data, clinical variables, and all data derived from dependent variables were analyzed descriptively. The measures of dependent variables at baseline (T0) and after the intervention (T8) were compared within each group with the paired t tests or the Wilcoxon test. The mean difference between the groups was calculated with a 95% confidence interval. Intergroup differences were calculated using Kruskal-Wallis test with post hoc Mann Whitney U testing and the general linear models of repeated measures (ANOVA of repeated measures) using the terms of group, time, and group versus time interaction with Bonferroni post hoc. The eta-square (η^2) values were calculated as a measure of the effect size between the groups (intergroup difference), and the results were interpreted as small (> 0.01), medium (< 0.06), and large (> 0.14) [17, 18]. The chi-square test was used to compare the distributions of the categorical variables.

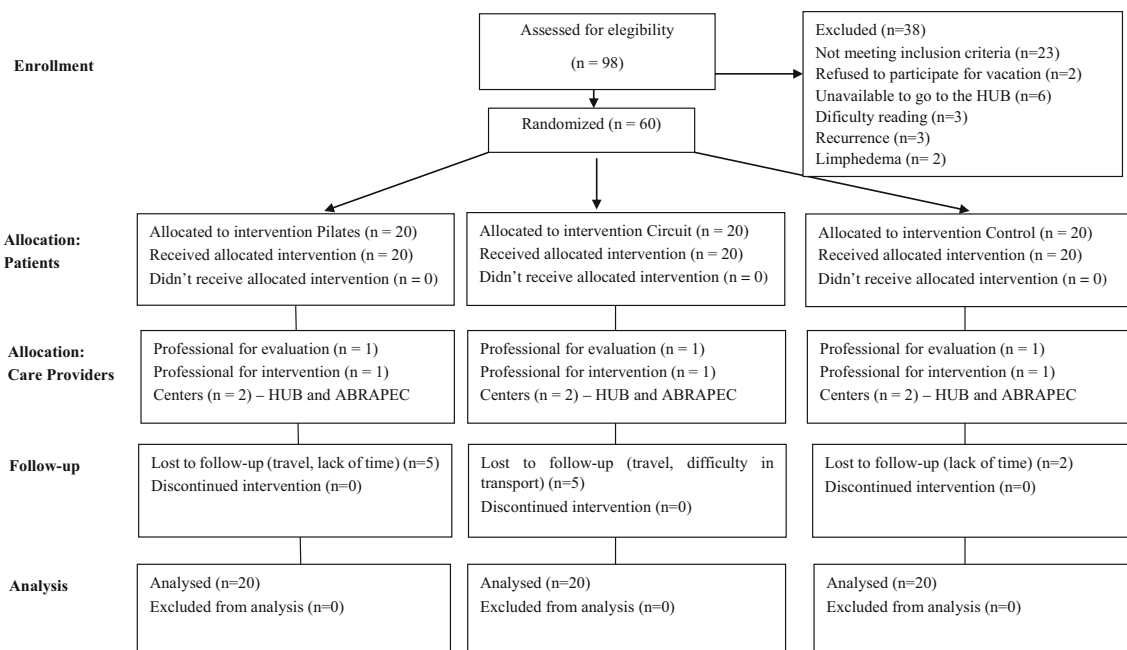


Fig. 1 CONSORT flow diagram

Table 1 Description of the exercises in the Pilates group and circuit-based exercise group

| | Pilates group | Circuit group |
|------------------|---|--|
| Intervention | 8 weeks | 8 weeks |
| Frequency | 2 times/week | 2 times/week |
| Session duration | 75 min | 75 min |
| Programming | 10' heating: exercise joint mobility or global stretching 60' Pilates – 07 basics exercises: - Breath with powerhouse activation - Flexion/extension of shoulders - Postural education - Sitting exercises - Stretching exercises - Training of proprioception 5' global stretching | 15' heating: exercise joint mobility or global stretching 50' circuit: 06 station - Aerobic exercise: step - Exercise for elbow flexion - Exercise for lower limbs - Exercise for shoulder - Exercise for lower limbs - Exercise for triceps 10' global stretching |
| Stimuli | 1 st and 2 nd initial week (basic exercises): 8 to 10 repetitions 3 rd to 8 th week (basic exercises with variations) | 1 st to 4 th week: 1 minute/station (25 to 30 repetitions) – 3 times 4 th to 8 th week: one min and 30 s – 3 times Monitoring: HR 60%-80% HR max |
| Instruments | - Ball of 26 inches - Elastic band | - Step - Elastic Band - Chair of 43 cm |
| References | Çakmakçı (2012); Kuçukçakir et al. (2013) [14–16] | MESH (2015); Bocalini et al. (2012) |

To investigate the Pilates group's effect of confounding variables, ANCOVA test was performed.

An intention-to-treat analysis was carried out on all outcome measures, handling missing data with the last observation carried forward approach, preserving balance offered by randomization. Statistical analyses were performed using SPSS software (IBM version 23.0, Chicago). Significance was recognized when $p < 0.05$.

Results

A total of 98 women complaining of arthralgia after breast cancer treatment were evaluated (Fig. 1). Of these 98 women, 23 did not meet the inclusion criteria, 8 reported limitation to physical exercise, two reported lymphedema, three had reading difficulties, and three had cancer recurrence. With 38 ineligible women, the remaining 60 women were randomized, 20 for each group (Fig. 1).

Baseline characteristics

The average age of study participants was 53.5 years. A majority of the participants had been diagnosed with stage II breast cancer (64.9%). The average time between diagnosis

and enrollment was 3.4 years (Table 2). There was no statistically or clinically important difference between groups at baseline. In the baseline characteristics, there was a significant difference only for sleep. The dropout participants showed worse sleep quality ($p < 0.05$).

Intervention adherence

The calculation for adherence was performed by the total number for sessions, and the minimum of 75% of presence was considered for each participant. The average adherence of the participants to the study was 83.44% for the Pilates group, 85.31% for the circuit-based exercise group, and 100% for control group. The reasons reported for exercise absence included travel and difficulty in obtaining transportation. Twelve participants had lost to follow-up, but all 60 participants were analyzed according to the intention-to-treat principal, preserving balance offered by randomization.

Effect of exercise on arthralgia

The median pain at baseline was homogeneous for the three groups. After 8 weeks, a two-point reduction in median pain was observed in the Pilates group, and a 0.5-point reduction was observed in the circuit-based exercise group and in the

Table 2 Sociodemographic and clinical characteristics of women with arthralgia in tamoxifen and anastrozole ($n=60$)

| | Pilates group | Circuit-based exercise group | Control group | <i>p</i> |
|--|---------------------|------------------------------|--------------------|----------|
| Characteristics | | | | |
| Years, months (median and interquartile) ^a | 52.0 [47.25; 61.50] | 54.0 [46.50; 60.75] | 59.8 [46.0; 59.0] | 0.898 |
| Marital status (% of total) ^b | | | | 0.668 |
| Single | 5.0 | 10.0 | 6.7 | |
| Married | 11.7 | 11.7 | 18.3 | |
| Divorced | 8.3 | 6.7 | 6.7 | |
| Stable union | 3.3 | 1.7 | 1.7 | |
| Widow | 5.0 | 3.3 | 0.0 | |
| Education (% of total) ^b | | | | 0.887 |
| Incomplete primary education | 13.3 | 11.7 | 10.0 | |
| Complete primary education | 5.0 | 1.7 | 3.3 | |
| Incomplete high school | 3.3 | 5.0 | 1.7 | |
| Complete high school | 6.7 | 6.7 | 10.0 | |
| Incomplete higher education | 0.0 | 3.3 | 1.7 | |
| Complete higher education | 5.0 | 5.0 | 6.7 | |
| Occupation (% of total) ^b | | | | 0.555 |
| Unemployed | 0.0 | 1.7 | 0.0 | |
| Employed | 10.0 | 5.0 | 10.0 | |
| Housewife | 21.7 | 26.7 | 20.0 | |
| Retired | 1.7 | 0.0 | 1.7 | |
| Student | 0.0 | 0.0 | 1.7 | |
| Cancer stage (% of total) ^b | | | | 0.784 |
| I | 6.7 | 11.7 | 8.3 | |
| II | 23.3 | 18.3 | 23.3 | |
| III | 3.3 | 3.3 | 1.7 | |
| Type of surgery (% of total) ^b | | | | 0.699 |
| Mastectomy | 26.7 | 21.7 | 26.7 | |
| Quadrantectomy | 3.3 | 8.3 | 5.0 | |
| Tumorectomy | 3.3 | 3.3 | 1.7 | |
| Chemotherapy (% of total) ^b | | | | 0.766 |
| YES | 26.7 | 23.3 | 25.0 | |
| NO | 6.7 | 10.0 | 8.3 | |
| Radiation therapy (% of total) ^b | | | | 0.931 |
| YES | 21.7 | 21.7 | 20.0 | |
| NO | 11.7 | 11.7 | 13.3 | |
| Hormonotherapy (% of total) ^b | | | | 0.932 |
| Tamoxifen | 20.0 | 20.0 | 21.7 | |
| Anastrozole | 13.3 | 13.3 | 11.7 | |
| Time of Hormonotherapy, months (median and interquartile) ^a | 20.5 [6.0; 28.0] | 17.5 [8.0; 24.0] | 18.0 [10.5; 25.50] | 0.937 |
| Time since diagnosis, years (median and interquartile) ^a | 4.0 [2.0; 5.0] | 3.0 [2.0; 4.0] | 3.0 [2.0; 4.0] | 0.589 |
| Time of pain, months (median and interquartile) ^a | 17.5 [4.50; 24.0] | 12.0 [6.0; 23.50] | 15.0 [6.50; 24.0] | 0.935 |
| Location of pain ^{bc} | | | | 0.538 |
| Upper members | 95 | 100 | 100 | |
| Lower members | 90 | 80 | 95 | |
| Pain medication ^{bc} | | | | 0.783 |
| Analgesic | 40 | 35 | 50 | |
| Glucosamine and chondroitin | 5 | 5 | 0 | |
| Does not use medication | 55 | 60 | 50 | |

^a Kruskal Wallis Test; ^b chi-square Pearson test; ^c percentage

control group (Table 3). The Pilates group demonstrated an improved minimum clinically important difference (MCID) and a statistically significant difference in pain reduction compared to the circuit training group (Table 4; Fig. 2). Even in the analysis for the chemotherapy, radiotherapy, and sleep covariables, the effect of the Pilates group remained the same.

The three groups were homogeneous at baseline in upper limb function measured with the DASH questionnaire. After 8 weeks, there was a decrease of 8.31 points between the Pilates and circuit-based exercise groups (Table 4).

In addition, there were no significant differences between the three groups for function, quality of sleep, and flexibility (Table 4).

Effect of exercise intragroup

The Pilates group had reduced average DASH questionnaire scores, quality of sleep, and flexibility after 8 weeks. The circuit-based exercise group had a 1.65-point reduced average quality of sleep after 8 weeks (Table 3).

Use of pain medications and adverse effects

At baseline, the 60 participants were asked about their use of pain medication via the BPI (Table 2). Participants were

followed up by telephone and evaluated via BPI after 8 weeks to monitor their use of medications during the trial. After 8 weeks of intervention, 55% of the participants in the Pilates group continued without medication: 25% stopped taking analgesics, and 5% stopped taking glucosamine and chondroitin. In the circuit-based exercise group, 60% continued without medication: 20% stopped taking analgesics, and 5% stopped taking glucosamine and chondroitin. In the control group, 50% continued without medication: 25% stopped taking analgesics. Participants reported that they stopped their use of pain medication when they noticed pain reduction or remission. Adverse events related to exercise were recorded. One participant reported back pain during the first week of intervention.

Discussion

In this clinical trial, we found that Pilates reduces pain score after 8 weeks in women with hormone therapy-induced arthralgia when compared with women in circuit-based exercise. These results are important for breast cancer survivors receiving hormone therapy because arthralgia has been a cause of low adherence to this treatment [19], which reinforces the need for strategies for arthralgia control [2].

Table 3 Intragroup and intergroup comparison on pain, function, sleep, and flexibility

| Outcome | Pilates group | Circuit group | Control group | Time | Interaction | Group |
|---------------------------------|-------------------|-------------------|-------------------|------------------------------|------------------------------|------------------------------|
| Pain^{cd} | | | | | | |
| Baseline (T0) | 5.00 [3.25; 6.75] | 5.00 [3.25; 6.00] | 5.00 [3.25; 7.75] | - | - | $p^b=0.962^{**}$ |
| Post intervention (T8) | 3.00 [1.00; 4.75] | 4.50 [3.00; 7.00] | 4.50 [1.50; 7.00] | - | - | $p^b=0.045^*$ |
| p^a | 0.001* | 0.305** | 0.254** | | | |
| Function^{ab} | | | | | | |
| Baseline (T0) | 35.68 (18.40) | 37.37 (18.84) | 37.47 (21.26) | F(1.57)=0.285; $p=0.596$ | F(2.57)=3.251; $p=0.046^*$ | F(2.57)=0.564; $p^b=0.572$ |
| Post intervention (T8) | 29.95 (14.29) | 38.26 (21.87) | 40.06 (22.85) | eta-square=0.005; power=0.08 | eta-square=0.102; power=0.60 | eta-square=0.019; power=0.14 |
| p^a | 0.036* | 0.727** | 0.265** | | | |
| Sleep^{ab} | | | | | | |
| Baseline (T0) | 10.20 (4.89) | 10.35 (5.15) | 10.85 (4.28) | F(1.57)=5.275; $p=0.025^*$ | F(2.57)=7.467; $p=0.001^*$ | F(1.57)=; $p^b=0.302$ |
| Post intervention (T8) | 8.35 (5.12) | 8.70 (5.19) | 11.95 (4.59) | eta-square=0.08; power=0.62 | eta-square=0.21; power=0.93 | eta-square=0.041; power=0.25 |
| p^a | 0.009* | 0.002* | 0.128** | | | |
| Flexibility^{ab} | | | | | | |
| Baseline (T0) | 20.02 (6.23) | 21.85 (8.02) | 20.98 (7.20) | F(1.57)=5.274; $p=0.025^*$ | F(2.57)=6.173; $p=0.558$ | F(1.57)=0.196; $p^b=0.822$ |
| Post intervention (T8) | 22.25 (6.53) | 23.00 (7.88) | 21.67 (8.19) | eta-square=0.085; power=0.62 | eta-square=0.02; power=0.14 | eta-square=0.007; power=0.07 |
| p^a | 0.022* | 0.151** | 0.607** | | | |

p^b = intergroup comparison. * p -value<0.05. p^a = comparison intragroup. ** p -value>0.05

Pain, numerical categorical scale; function, disabilities of the arm, shoulder, and hand; sleep, Pittsburgh Sleep Quality Index; flexibility, Wells bench. Average values (standard deviation). Mean or median values [percentile 25%; 75%]. ^aANOVA of repeated measures test. ^bStudent *t*-test for paired samples. ^cKruskal-Wallis test. ^dWilcoxon test for paired samples

Table 4 Comparison of mean difference on pain, upper limb function, sleep quality, and flexibility between groups at baseline and after 8 weeks of intervention

| Outcomes | Pilates | Circuit | Control | Pilates × circuit ^c | Effect size | p | Pilates × control ^c | Effect size | p | Circuit × control ^c | Effect size | p |
|---------------------------------|----------------------|----------------------|----------------------|--------------------------------|----------------|----------------|--------------------------------|-----------------|-----------------|--------------------------------|-----------------|-----------------|
| Pain^{ac} | | | | | | | | | | | | |
| Baseline | 5.00 [3.25; 6.75] | 5.00 [3.25; 6.75] | 5.00 [3.25; 6.00] | -0.05 [-1.13; 1.03] | 0.912** | 0.020* | -0.20 [-1.53; 1.13] | 0.783** | 0.055*** | -0.15 [-1.53; 1.23] | 0.869** | 0.678** |
| 8 weeks | 3.00 [1.00; 4.75] | 4.50 [3.00; 7.00] | 4.50 [1.50; 7.00] | -1.95 [-3.45; -0.45] | 0.83*** | 0.59† | -1.60 [-3.34; 0.14] | 0.055*** | 0.13† | 0.35 [-1.31; 2.01] | 0.13† | 0.678** |
| Function^{bd} | | | | | | | | | | | | |
| Baseline | 35.68 [27.07; 44.29] | 37.37 [28.55; 46.19] | 37.47 [27.52; 47.42] | -1.69 [-13.61; 10.23] | 1.000** | 0.585** | -1.79 [-14.51; 10.94] | 1.000** | 0.53† | -0.10 [-12.95; 12.76] | 1.000** | 1.000** |
| 8 weeks | 29.95 [23.27; 36.64] | 38.60 [28.02; 48.49] | 40.06 [29.36; 50.75] | -8.31 [-20.13; 3.52] | 0.45† | 0.74† | -10.10 [-22.30; 2.09] | 0.349*** | 0.08† | -1.80 [-16.12; 2.52] | 0.349*** | 1.000** |
| Sleep^{bd} | | | | | | | | | | | | |
| Baseline | 10.20 [7.91; 12.49] | 10.35 [7.94; 12.76] | 10.85 [8.84; 12.85] | -0.15 [-3.37; 3.07] | 1.000** | 1.000** | -0.65 [-3.59; 2.29] | 1.000** | 1.000** | -0.50 [-3.53; 2.53] | 1.000** | 1.000** |
| 8 weeks | 8.35 [5.95; 10.75] | 8.70 [6.27; 11.13] | 11.95 [9.80; 14.10] | -0.35 [-3.65; 2.95] | 0.07† | 0.74† | -3.60 [-6.71; 0.48] | 0.078*** | 0.66† | -3.25 [-6.39; -0.11] | 0.078*** | 0.130*** |
| Flexibility^{bd} | | | | | | | | | | | | |
| Baseline | 20.02 [17.11; 22.94] | 21.85 [18.09; 25.60] | 20.98 [17.61; 24.35] | -1.82 [-6.42; 2.77] | 1.000** | 1.000** | -0.95 [-5.27; 3.36] | 1.000** | 1.000** | 0.87 [-4.01; 5.75] | 1.000** | 1.000** |
| 8 weeks | 22.25 [19.19; 25.31] | 23.00 [19.31; 26.69] | 21.67 [17.84; 25.51] | -0.75 [-5.38; 3.88] | 0.10† | 0.08† | 0.57 [-4.17; 5.32] | 1.000** | 0.16† | 1.32 [-3.82; 6.47] | 1.000** | 1.000** |

^a Median [CI 95%]. ^b Mean [CI 95%]. ^c Mean difference [CI 95%]. ^d Bonferroni post hoc. ^e Mann Whitney U post hoc. [†] Small effect size. [‡] Medium effect size. ^{***} Large effect size. *p-value<0.05. **p-value>0.05

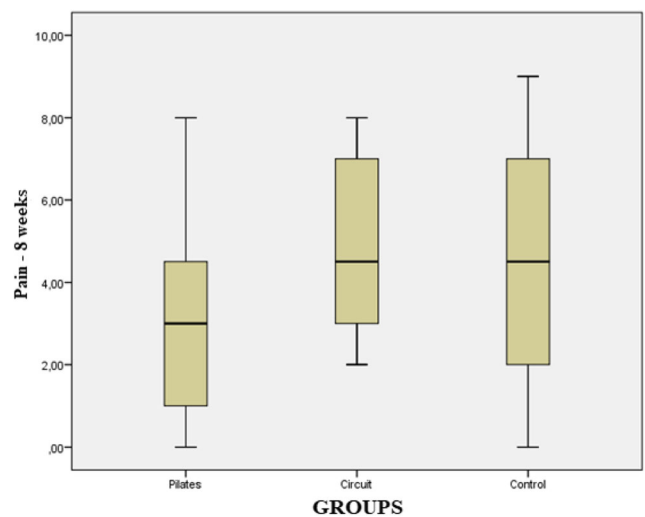


Fig. 2 Groups after 8 weeks

Treatments for arthralgia have been reported in the literature; however, most studies have small sample sizes and high risks of bias [3]. To our knowledge, no other randomized trial has compared Pilates to circuit training for arthralgia in breast cancer survivors undergoing hormone therapy. The ideal type, frequency, and duration of exercise for women with hormone-induced arthralgia are unknown [20].

A recent meta-analysis reported a controversial finding about the benefits of physical exercise in reducing arthralgia. Irwin et al. [7] performed a clinical trial with 121 women on aromatase inhibitor therapy and found that a combination of aerobic and resistance exercises was effective for reducing aromatase inhibitor-induced arthralgia after 12 months. However, other studies that investigated the use of Nordic-Trac walking or a combination of aerobic and resistance exercises did not find exercise beneficial for hormone-induced arthralgia [21].

The mechanism of hormone-induced arthralgia is not completely understood. Although it has no well-known effects on joints, estrogen may influence the neural processing of nociceptive input and specifically affect inflammatory cytokines [22, 23]. Thus, it is possible that a rapid fall in estrogen, which occurs during hormone therapy, provides a direct nociceptive stimulus to the joints and/or removes the anti-nociceptive protective role of estrogen, exposing those women to joint pathology [23]. The mechanisms through which exercise could improve arthralgia are not entirely clear, either [7]. Exercise improves blood flow to tissues, increases maximal oxygen consumption [24], and increases pain threshold [25]. Aerobic exercise involves the rapidly alternating contraction of large muscle groups with low resistance for a sustained period. This type of training leads to increased mitochondrial activity and increased blood flow to the muscle because of increased numbers of capillaries and improved efficiency of blood flow [26]. Endurance activity increases

beta-endorphins in the plasma and endogenous chemicals found in the central nervous system that are released to relieve pain [27].

In the present study, a reduction in pain was observed in women who performed Pilates compared to those completing circuit training. Positive results with Pilates can be attributed to improved joint mobility [28] and the fact that Pilates has been used by women with chronic pain due to fibromyalgia [28, 29] because it focuses on isometric contractions and causes less fatigue than aerobic exercise [28]. As women with breast cancer also feel fatigued during hormone therapy [1], we believe that women with hormone-induced arthralgia will benefit more from Pilates than circuit-based exercise.

We did not observe significant difference on function, sleep quality, or flexibility when comparing the three groups. Pinto-Carral et al. [5] reported that Pilates was statistically more effective than other interventions in improving the function of upper limbs of women with breast cancer [5]. In agreement with our study, Zengin et al. [30] did not observe a significant improvement of function via DASH when comparing the effectiveness of Pilates, combined exercises, and home exercises in women with breast cancer [30]. Quality of sleep was evaluated in a meta-analysis by Zhu et al. [31] who reported no significant difference in breast cancer survivors between groups with exercise interventions [31], which also corroborates our results and reinforces the need for further studies to assess this outcome in breast cancer. Flexibility was evaluated by Eyigor et al. [8] who reported efficacy of Pilates in patients with breast cancer. The authors did not observe increases in women's flexibility after 8 weeks of intervention [8], which corroborates our results. However, in healthy people, Pilates has shown obvious benefits for flexibility [32, 33]. Although the present study did not demonstrate significant differences in function, sleep quality, or flexibility when comparing the three groups, we did observe improvement in these outcomes after 8 weeks of Pilates intervention.

Our study has limitations that should be pointed out. We did not long term follow up on these participants. However, the major strength of the present study is the fact that it is the first parallel arm trial comparing the effect of Pilates and circuit-based exercise on hormone-induced arthralgia relative to control. Our study was randomized with concealed allocation, evaluator blinding, and intention-to-treat analysis, according to CONSORT.

Conclusion

Our study demonstrated that Pilates was more effective than circuit-based exercise in reducing women's arthralgia during hormone therapy for breast cancer.

Abbreviations ANOVA, Analysis of variance; BMI, Body mass index; CONSORT, Consolidated Standards of Reporting Trials; DASH, Disabilities of the arm, shoulder, and hand questionnaire; NRS, Numerical rating scales; BPI, Brief pain inventory; RCT, Randomized controlled trial; PSQI, Pittsburgh Sleep Quality Index; PAR-Q, Questionnaire of readiness for physical activity

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Code availability Not applicable

Author contribution All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Keyla de Paula Barbosa, Lidiane Gomes Tavares da Silva, Patrícia Azevedo Garcia, Cariele de Aguiar Freitas, Ellen Cristine Ferreira da Silva, Thiago Vidal Pereira, Aline Teixeira Alves, and Liana Barbaresco Gomide Matheus. The first draft of the manuscript was written by Keyla de Paula Barbosa, Lidiane Gomes Tavares da Silva, and Liana Barbaresco Gomide Matheus, and all authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability All data and materials are available.

Declarations

Ethics approval Protocol Number - 2.889.890

Consent to participate Written informed consent was obtained from all participants.

Consent for publication All authors agree with the publication (authorship form).

Conflict of interest The authors declare no competing interests.

References

1. Howell PA (2005) Results of the ATAC (Arimidex , Tamoxifen , Alone or in Combination) trial after completion of 5 years ' adjuvant. *Lancet* 365:60–62
2. Coleman RE, Bolten WW, Lansdown M, Merkel D, Maass N, Hadji P, et al (2008). Aromatase inhibitor-induced arthralgia: clinical experience and treatment recommendations. *Cancer Treat Rev* 275–82.
3. Roberts K, Rickett K, Greer R, Woodward N (2017). Management of aromatase inhibitor induced musculoskeletal symptoms in postmenopausal early breast cancer: a systematic review and meta-analysis. *Crit Rev Oncol / Hematol* [Internet]. 111:66–80. Available from: <https://doi.org/10.1016/j.critrevonc.2017.01.010>
4. Mazzarino M, Midwifery MC, Kerr D, Philosophy D, Wajswelner H, Doctorate C, et al (2015). Pilates method for women's health: systematic review of randomized controlled trials. *Arch Phys Med Rehabil* [Internet]. Available from: <https://doi.org/10.1016/j.apmr.2015.04.005>

5. Pinto-carral A, Molina AJ, De Pedro Á, Ayán C (2018). Pilates for women with breast cancer: a systematic review and meta-analysis. *Complement Ther Med* [Internet] 41:130–40. Available from: <https://doi.org/10.1016/j.ctim.2018.09.011>
6. Nikander R, Sievänen H, Ojala K, Oivanen T, Pirkko-Liisa, Kellokumpu-Lehtinen et al (2007) Effect of a vigorous aerobic regimen on physical performance in breast cancer patients — a randomized controlled pilot trial. *Acta Oncol (Madr)* 46:181–186
7. Irwin ML, Cartmel B, Gross CP, Ercolano E, Li F, Yao X, Fiellin M, Capozza S, Rothbard M, Zhou Y, Harrigan M, Sanft T, Schmitz K, Neogi T, Hershman D, Ligibel J (2015) Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer survivors. *J Clin Oncol* 33(10):1104–1111
8. Eyigor S, Karapolat H, Yesil H, Uslu R, Durmaz B (2010) Effects of pilates exercises on functional capacity, flexibility, fatigue, depression and quality of life in female breast cancer patients: a randomized controlled study C ER IG E IN. *Phys Med Rehabil Clin N Am* 46(4):481–487
9. Hjemstad M, Fayers P, Haugen D (2011). Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review 41(6):1073–93.
10. Cleeland CSRK (1994) Pain assessment: global use of the brief pain inventory. *Ann Acad Med Singapore*. 23:129–138
11. Kennedy CA, Beaton DE S S (2011). *Disabilities of the arm, shoulder and hand (DASH): the DASH and QuickDASH outcome measure user's manual* (ed 3). Institute for Work and Health. Toronto, Ontario, Canada; 2011
12. Orfale AG, Ferraz MB, Natour J, De Reumatologia D, De Medicina EP (2005) Translation into Brazilian Portuguese , cultural adaptation and evaluation of the reliability of the disabilities of the arm , shoulder and hand questionnaire. *Brazilian J Med Biol Res* 38:293–302
13. Bertolazi AN, Fagondes SC, Hoff LS, Dartora EG, da Silva Miozzo IC, de Barba MEF, Menna Barreto SS (2011) Validation of the Brazilian Portuguese version of the Pittsburgh Sleep Quality Index. *Sleep Med* 12(1):70–75
14. Evrim Ç (2012) The effect of 10 week pilates mat exercise program on weight loss and body composition for overweight Turkish women. *World Appl Sci J*. 19(3):431–438
15. Kuçukçakir N, Altan L, Korkmaz N (2013) Effects of Pilates exercises on pain , functional status and quality of life in women with postmenopausal osteoporosis. *J Bodyw Mov Ther* 17:204–211
16. Bocalini DS, Lima LS, de Andrade S, Madureira A, Rica RL, dos Santos RN et al (2012) Effects of circuit-based exercise programs on the body composition of elderly obese women. *Clin Interv Aging* 7:551–556
17. Cohen J (1998) *Statistical power analysis for the behavioral sciences*. NY Routledge Acad, New York
18. Lakens D (2013). Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t -tests and ANOVAs. 4: 1–12.
19. Dowsett M, Cuzick J, Ingle J, Coates A, Forbes J, Bliss J, et al (2010). Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen 28(3):509–18.
20. Fields J, Richardson A, Hopkinson J (2016). Nordic walking as an exercise intervention to reduce pain in women with aromatase inhibitor e associated arthralgia: a feasibility study. *j pain symptom manage* [Internet] 52(4):548–59. Available from: <https://doi.org/10.1016/j.jpainsymman.2016.03.010>
21. Lohrisch CA, McKenzie D, Truong P, Jespersen D, Gelmon KA, Premji S, Kennecke HF (2011) Randomized trial of exercise versus control for musculoskeletal symptoms from adjuvant anastrozole (A) for postmenopausal early breastcancer (PEBC). *J Clin Oncol* 29(15):636
22. D' Agostino P, Milano S, Barbera C, Di Bella G, La Rosa M, Ferlazzo V, et al (1996). Sex hormones modulate inflammatory mediators produced by macrophages p. 426–9.
23. Felson DT, Cummings SR (2005) Aromatase inhibitors and the syndrome of arthralgias with estrogen deprivation. *ARTHRITIS Rheum* 52(9):2594–2598
24. Church TS, Earnest CP, Skinner JS, Blair SN (2007). Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure a randomized controlled trial. *JAMA* [Internet] 16;297(19):2081–91. Available from: <https://doi.org/10.1001/jama.297.19.2081>
25. Jones MD, Booth J, Taylor JL, Barry BK (2014) Aerobic training increases pain tolerance in healthy individuals. *Med Sci Sport Exerc* 31:1640–1647
26. Holloszy JO (1975) Adaptation of skeletal muscle to endurance exercise. *Med Sci Sport*. 7(3):155–164
27. Bender T, Nagy G, Barna I, Tefner I, Kádás É, Géher P (2007) The effect of physical therapy on beta-endorphin levels. *Eur J Appl Physiol* 100:371–382
28. Altan L, Korkmaz N, Bingol U, G B (2009). Effect of Pilates training on people with fibromyalgia syndrome: a pilot study. *YAPMR* [Internet] 90(12):1983–8. Available from: <https://doi.org/10.1016/j.apmr.2009.06.021>
29. Hamilton NA, Affleck G, Tennen H, Karlson C, Luxton D, Preacher KJ, et al (2008). Fibromyalgia: the role of sleep in affect and in negative event reactivity and recovery 27(4):490–4.
30. Zengin Alpozgen A, Razak AA, Pt O, Karanlik H, Agaoglu AFY, Pt ANN (2017). Effectiveness of Pilates- based exercises on upper extremity disorders related with breast cancer treatment 1–8.
31. Yu Z, Guo X, Jiang Y, Teng L, Luo J (2018) Adjuvant endocrine monotherapy for postmenopausal early breast cancer patients with hormone-receptor positive: a systemic review and network meta-analysis. *Breast Cancer* 25(1):8–16
32. Pirunsan SPAPU, Silitertpisan P (2011) Effects of Pilates training on lumbo-pelvic stability and flexibility. *Sport Med Res Cent* 2(1): 16–22
33. Cruz-Ferreira A, Fernandes J, Laranjo L, Bernardo LM, Silva A (2011). A systematic review of the effects of pilates method of exercise in healthy people. *Arch Phys Med Rehabil* [Internet] 92(12):2071–81. Available from: <https://doi.org/10.1016/j.apmr.2011.06.018>

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