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Improved self-esteem after mat Pilates method intervention in breast cancer women undergoing hormone therapy: randomized clinical trial pilot study

Melhora da autoestima após intervenção do método Pilates solo em mulheres com câncer de mama em tratamento de hormonioterapia: ensaio clínico randomizado estudo piloto

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Abstract - The purpose of this randomized clinical trial was to analyze the effects of 16 weeks of mat Pilates method intervention in self-esteem and depressive symptoms in women with breast cancer undergoing hormone therapy. Thirty-four women were randomized in Pilates group (PG) (n=18) and control group (CG) (n=16). The intervention occurs for 16 weeks, three times per week for 60 minutes each session (light to very hard intensity according to BORG scale). The CG received three educational sessions and was invited to maintain their routine activities. The data collection took place at the baseline and post-intervention. A questionnaire was applied including Self-Esteem Scale and the Beck Depression Inventory. Anova Two way with repeated measures and Sydak comparison test was used to analyze the effects in the variables after the 16 weeks intervention. Two types of analysis were performed after the intervention, in the analysis by intention to treat PG (n=18) the self-esteem variable showed a significant result (p=0.011) and in the analysis by PG protocol (n=11) (p=0.013). The depressive symptoms did not demonstrate significant improvements after the intervention. Control group did not present any significant changes during the time of the study. The 16 weeks of PG was an effective intervention to improve self-esteem of women with breast cancer undergoing hormone therapy. Keywords: Breast neoplasm; Physical activity; Pilates; Self-esteem; Depression.

Resumo - O objetivo deste ensaio clínico randomizado foi analisar o efeito de 16 semanas de intervenção do método Pilates na autoestima e sintomas depressivos em mulheres com câncer de mama em terapia hormonal. Trinta e quatro mulheres foram randomizadas no grupo Pilates (PG) (n = 18) e no grupo controle (GC) (n = 16). A intervenção ocorre por 16 semanas, com 3x por semana, durante 60 minutos cada sessão (intensidade leve a intenso de acordo com a escala de BORG). O GC recebeu atividades educativas em forma de palestras e foi convidado a manter suas atividades de rotina. A coleta de dados ocorreu na linha de base e pós-intervenção. Foi aplicado um questionário incluindo a Escala de Autoestima e o Inventário de Depressão de Beck. Anova Two way, com medidas repetidas e teste de comparação de Sydak, foi utilizado para analisar os efeitos nas variáveis após as 16 semanas de intervenção. Dois tipos de análise foram realizados após a intervenção, na análise por intenção de tratar PG (n=18) a variável autoestima apresentou resultado significativo (p=0.011) e na análise por protocolo PG (n=11) (p=0.013). Os sintomas depressivos não demonstraram melhora significativas após a intervenção. O grupo controle não apresentou alterações significativas durante o período do estudo. As 16 semanas de PG foram uma intervenção eficaz para melhorar a autoestima de mulheres com câncer de mama em terapia hormonal. Palavras-chave: Atividade física; Autoestima; Câncer de mama; Depressão; Pilates.

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INTRODUCTION

Breast cancer is more prevalent in women and represents 30% of all types of cancer in the world¹. According to the Brazilian National Cancer Institute (INCA)² for the 2020-2022 triennium, 66,280 new cases of breast cancer are estimated for each year in Brazil.

For women, the breast represents the feeling of femininity and sexuality, and breast cancer surgery may imply feeling of mutilation and aggression against their self-esteem³. These women may also develop depression triggered by inferiority, fear, anxiety and rejection after breast cancer surgery and clinical treatments^{4,5}. Systematic review and meta-analysis concluded that physical activity has positive effects on psychological aspects in cancer patients⁶ and it can help improve the sequelae caused by the treatment, such as fatigue, muscle strength, pain, range of motion, upper limb, functionality, proprioception and quality of life^{6,7}.

Some evidences show that physical exercise has a positive effect against self-esteem and depressive symptoms in women with breast cancer, with the release of dopamine and endorphin, hormones responsible for a relaxing and well-being effect^{8,9}. The Pilates method, involves mental and physical exercises which are safe for the exercises are performed lying down thus reducing the impact on the body and the intensity of the exercises can be graded according to the resistance of each woman, being an effective and viable option to improve the health conditions of these women¹⁰.

Some studies indicate positive improvements in well-being after practicing the Pilates method among women with breast cancer in their quality of life, mood, body image, fatigue, depressive symptoms, pain, range of motion of the upper limb and consequently contributes to the improvement of upper limb functionality¹¹⁻¹³. It is recommended for women with breast cancer to engage in at least 150 minutes of moderate to vigorous physical activity per week and include muscle strengthening exercises at least twice a week¹⁴.

Despite the number of positive benefits about physical activity and breast cancer found in a Systematic Review and Meta-analysis⁸, it is not yet known the effects of 16-weeks Pilates method in self-esteem and depressive symptoms. Thus, the findings of this study may help health professionals to include a different physical activity modality for woman with breast cancer in the oncology setting, increasing their practice of regular physical activity. Our hypothesis in this study is that the intervention of the mat Pilates method may improve the depressive and self-esteem symptoms among women with breast cancer. The objective of this randomized clinical trial is analyzing the effects of a 16 week Pilates method intervention in self-esteem and depressive symptoms in women with breast cancer undergoing hormone therapy.

METHOD

Trial design

This is a randomized clinical trial with two-arm trial (intervention with Mat Pilates methods and control group) conducted in Brazil. It follows two arms from the three arms protocol from Boing et al. ¹⁵ and is part of the MoveMama study. This study contains the primary results of the MoveMama study, in which

we are evaluating only two-arm trial. The study was approved by the Committee on Ethics in Research in Human Beings (CEPSH) of UDESC, protocol no. 688.548 and by the Research Ethics Committee of CEPON (CEP), protocol number 818.174 and registered in Clinical Trials NCT03194997.

Participants

Eligible participants were women with breast cancer undergoing hormone therapy at the Oncology Research Center (CEPON) in Santa Catarina state in Brazil. The inclusion criteria were: (1) 18 years or older; (2) Stage 0 to III of breast cancer; (3) Authorization to exercise from the Physiotherapy department in CEPON. Exclusion criteria was defined as: (1) Diagnosis of some orthopedic or neurological limitation that prevents the practice of physical activity, such as Parkinson disease, Alzheimer's or use of a wheelchair.

Sample size

The sample size for this study was determined by using the G^* Power 3.1.9.2 16 , considering the significance level of 5%, test power of 80% and Cohen's effect size of 0.25, the sample size required was 34 participants.

Randomization

The randomization was performed by two researchers of the study and carried out via a website (http://www.randomization.com) which predicted the allocation of participants into three groups, being Pilates methods, belly dance and control group. However, for this study we only include Pilates methods and control group. The randomization was stratified by age, dividing the participants between those younger and those over 60 years, according to the Brazilian Statute of the Elderly, established by Law N° 10.741. dated October 1, 2003. More detailed information about the randomization process can be found in the protocol study¹⁵.

Group control

Women randomized to control group (n = 24) were invited to maintain the daily routine activities. During the 16 weeks of intervention, they were contacted by telephone two times (July and September 2018) in order to identify possible changes regarding physical exercise. These women also received three educational sessions to keep them motivated and welcomed in the study. The first occurred one week after the beginning of the intervention, in which they received guidance on active upper limb movements to be performed at home. The second educational session took place on the 8th week after the beginning of the intervention about self-esteem and body image with the report of another woman who had similar experiences, and the last one, a lecture took place on the 16th week on the theme of lymphedema prevention. At the end of the 16 weeks the control group received an explanatory booklet prepared by researchers from LAPLAF/CNPq about the benefits of daily physical activity for breast cancer survivors.

Interventions group

Women randomized to Pilates group (n = 25) were submitted to mat Pilates methods group sessions held in the leisure space at CEPON in Brazil. All sessions were taught by a LAPLAF physiotherapist who followed the Mat Pilates methods protocol for participants with breast cancer¹⁵. Each session occurred in the morning, three times per week for 16 weeks (totaling 48 sessions) and each session lasted 60 minutes. The decision of 16 weeks of intervention was based on the systematic review of breast cancer and Pilates¹⁷. In this review, most of the studies provided 8 weeks interventions, three times per week and 45-60 min sessions. So, based on these findings, we decided to propose an innovative 16 weeks with three 60-minute sessions per week.

The first session was familiarization with the method and the teaching of all the principles (Concentration, Centering, Precision, Breathing, Control and Fluidity). The intervention exercises were progressive, and each session was divided into 20 minutes warm-up, 30 minutes main part and 10 minutes calm back. The intensity was according to BORG scale¹⁸. This scale ranges from six to 20 points, where position six would be perceived as "very light" and 20 as "exhaustive". At the end of every session the women were asked about the intensity of the classes, at the end of the 16 weeks we noticed that intensity varied from 7 (light) to intense/hard (15).

The warm-up and stretching includes breathing, imprint and release, hip release, spinal rotation, cat stretch, hip rolls, scapula isolation, arm circles, head nods, elevation and depression of scapulae exercises. The main paint started with a brief explanation of the purpose of the class, followed by the main exercises of Pilates methods described further in the published protocol¹⁵. To increase the load during the protocol, TheraBand and toning ball exercises was added at the 10th session, in the 20th arms exercise was added and from the 24th session the spinal rotation was performed with 1 kg weight. At the end of the session, the women were invited to sit on the ball, stretch the spine forward on the ball, self-stretching of cervical muscles on the ball (upper trapezius and scalene muscles), and active mobilization of the cervical spine.

The progression of upper limb movements respected the limits of each participant, and the progression of the exercises is described on the protocol study¹⁵. At the end of the intervention, in order to motivate them to stay physically active, this group also received the explanatory booklet about the benefits of daily physical activity practice for breast cancer survivors.

Outcomes

The main outcome for this randomized clinical trial was self-esteem and depressive symptoms.

For investigation of self-esteem the Self-Esteem Scale (SES) developed by Rosenberg¹⁹ was used, this scale was validated for the population in Brazil²⁰. It is a one-dimensional measure consisting of ten statements related to a set of self-esteem and self-acceptance feelings that determine the global self-esteem. The total scale score varies from 10 to 40 points. It is understood that the greater the value reached by the woman on the scale the better her self-esteem.

To assess the depressive symptoms of the women with breast cancer the Beck Depression Inventory (BDI) was used, a self-report questionnaire originally developed by Beck et al.²¹, it was validated in Brazil by Cunha²² and to breast cancer women by Gandini²³. It contains 21 multiple-choice objective questions related to depressive symptoms, in detail: sadness, pessimism, feeling of failure, dissatisfaction, guilty feelings, punishment feelings, self-dislike, self-criticism, suicidal thoughts, crying, irritability, withdrawal from family or friends. The sum of the scores of each question provides a total score, ranging from zero to 63, and the closer to 63, the greater the presence of depressive symptoms, indicating a higher degree of depression, and the greater the proximity to the zero the greater the absence of depressive symptoms.

A questionnaire was used to characterize the sample containing sociodemographic (age, educational status, marital status, and economic level), clinical (type of hormone therapy, surgery information, breast reconstruction, lymphedema by self-report, physiotherapy treatment). As an economic level the minimum wage was used according to the Brazilian Institute of Geography and Statistics (IBGE), and the women were classified into receiving less than two minimum wages and more than two minimum wages per month.

For anthropometric measurements, height was collected using a wall-mounted stadiometer (Sanny brand, height 2.0 m and 0.1 cm scale) and body mass by a digital scale (Toledo brand, model 2096 PP), capacity of 200kg and resolution of 50g) with the participants in standing position and bare feet. Body Mass Index (BMI) was assessed and identified by dividing body mass (Kg) and height square (m2). Participants with a BMI of up to 24.9 kg/m2 were categorized as adequate weight and above 25 kg/m2 as overweight or obese.

Data collection

All participants were invited to voluntarily participate in the study, and those who participated signed a Free and Informed Consent Term, assuring the rights of the participants as prescribed in Resolution 196/96 from the Brazilian National Health Council. The data collection was administered before the beginning of the intervention (baseline collection) and after the conclusion of the 16-week protocol (post-intervention collection). All the data collection took place at the Santa Catarina State University in Florianopolis, SC – Brazil. All the researchers were trained and applied the questionnaires in an interview format to each participant and lasted around 30 minutes with each one.

Adherence assessment

The adherence of the participant calculation was developed as follows: the number of sessions attended/48 planned sessions*100²⁴. The attendance was recorded by the researchers during the 16 weeks. The participants that did not attend a minimum of 50% of the sessions was collected and evaluated as intention to treat (ITT) analysis, and not as per protocol.

Statistical methods

All analyses were performed using IBM SPSS version 20.0.

To verify the sociodemographic and clinical characteristics between the two groups the descriptive analysis was used. To analyse the two groups in baseline and post intervention conditions it was used the Two-Way Anova with repeated measures and Sydak comparison test. The level of statistical significance adopted in the analyses was 5% and the Cohen effect size f2 was also used.

RESULTS

Forty-nine (n = 49) women with breast cancer undergoing hormone therapy were included in the study and randomized into two groups, 25 women in the PG and 24 women in the CG, with a 55 ± 11 years mean age. During the 16 weeks of intervention, seven women were lost in each randomized group; In the end, 18 women were analyzed as intention to treat in PG, and 11 according to protocol, and in the CG 16 women were analyzed. Detailed information can be found in Figure 1, which shows the flow diagram of all the phases of this randomized clinical trial.

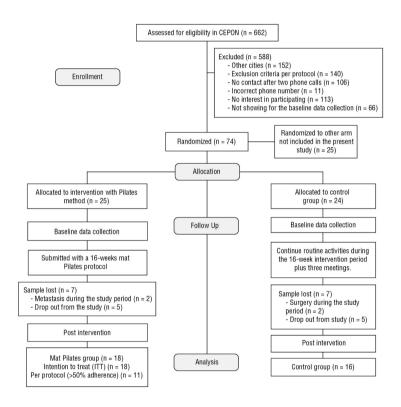


Figure 1. Flowchart of selection of participants for the randomized clinical trial, CONSORT-2010.

It was observed in the 34 women with breast cancer included in the study that most of them studied for more than nine years (65%), did not have a job (64%), did not have a partner (53%), received more than two minimum salaries (56%), were overweight or obese (65%), did not have any other comorbidities (68%), had received a breast-conserving surgery (60%), had a left side surgery (59%), were submitted to a lymphadenectomy (62%), did not undergo a breast reconstruction surgery (71%), and used the aromatase inhibitors as hormone therapy (65%), received radiotherapy (71%) and chemotherapy (91%) and did not present lymphedema (92%) (Table 1).

Table 1. Comparison between demographic and clinical variables at the time of randomization, according to the group ITT (n=34). Florianópolis, SC -2019.

Variables	Total N (%)	Group	n value		
variables	TOTAL IN (70)	GI (n=18)	GC (n=16)	p value	
Age					
Averege (DP)	55.29 (10.93)	53.33 (8.58)	57.50 (13.02)	0.274***	
Education					
Up to 8 years of study	12 (35.3%)	07 (58.3%)	05 (41.7%)	0.642*	
More than 9 years of study	22 (64.7%)	11 (50.0%)	11 (50.0%)	0.012	
Current occupation					
External work	12 (35.3%)	06 (50.0%)	06 (50.0%)	0.800*	
No external work	22 (64.7%)	12 (54.5%)	10 (45.5%)	0.000	
Marital status					
No companion	16 (47.1%)	08 (50.0%)	08 (50.0%)	0.746*	
With companion	18 (52.9%)	10 (55.6%)	08 (44.4%)	U./40	
Family income					
≤ 2 minimum wages	15 (44.1%)	09 (60.0%)	06 (40.0%)	0.464*	
> 2 minimum wages	19 (55.9%)	09 (47.4%)	10 (52.6%)	0.404	
ВМІ					
Adequate	12 (35.3%)	06 (50.0%)	06 (50.0%)	0.000*	
Overweight or obese	22 (64.7%)	12 (54.5%)	10 (45.5%)	0.800*	
Comorbidities					
Yes	11 (32.4%)	05 (45.5%)	06 (54.5%)	0.545*	
No	23 (67.6%)	13 (56.5%)	10 (43.5%)	0.545*	
Type of breast surgery					
Mastectomy	14 (41.2%)	09 (64.3%)	05 (35.7%)	0.707**	
Conservative	20 (58.8%)	09 (45.0%)	11 (55.0%)	0.727**	
Type of breast surgery					
Axillary Lymphadenectomy	21 (61.8%)	11 (52.4%)	10 (47.6%)		
Sentinel lymph nodes	05 (14.7%)	02 (40.0%)	03 (60.0%)	0.727*	
Not realized	08 (23.5%)	05 (62.5%)	03 (37.5%)		
Breast reconstruction	, ,	, ,	, ,		
No	24 (70.6%)	12 (50.0%)	12 (50.0%)	0.745++	
Yes	10 (29.4%)	06 (60.0%)	04 (40.0%)	0.715**	
Modality of Hormone therapy	,	,	,		
Aromatase inhibitors	22 (64.7%)	12 (54.5%)	10 (45.5%)		
Tamoxifen	12 (35.3%)	06 (50.0%)	06 (50.0%)	0.800*	
Radiotherapy preview	(((((((((((((((((((((**************************************	(00.07.7)		
No	10 (29.4%)	05 (50.0%)	05 (50.0%)	1.000**	
Yes	24 (70.6%)	13 (54.2%)	11 (45.8%)		
Chemotherapy preview	= : (, 0.0,0)	(= /-)	(. 3. 3 / 3 /		
No	03 (8.8%)	02 (66.7%)	01 (33.3%)	1.000**	
Yes	31 (91.2%)	16 (51.6%)	15 (48.4%)	1.000	
Lymphoedema	01 (01.270)	10 (01.070)	10 (10.170)		
Yes	6 (17.6%)	04 (66.7%)	02 (33.3%)		
No	28 (82.45)	14 (50.0%)	14 (50.0%)	0.660**	

Note. *Chi-Square Test; **Fisher's Exact Test; ***T test for independent samples.

In the PG adherence to intervention was of 68%, and the women allocated in the intention to treat analysis attended 19% of the sessions (data not shown in table).

In the intention to treat analysis, the self-esteem showed significant improvements for PG (p = 0.011), as well the intervention size effect was strong (f2 = 0.85). No significant results were demonstrated in this analysis for depressive symptoms (Table 2).

In Table 3 the results were observed per protocol analysis after the 16 weeks of intervention. It was found significant improvements in self-esteem (p = 0.013), and strong effect size for this variable (f2 = 1.08). For depressive symptoms no

significant improvements were shown. There were no significant differences between PG and CG in the post intervention.

Table 2. Intention to treat analysis for self-esteem and depressive symptoms between Pilates method group and control group (n = 34). Florianopolis, SC – Brazil, 2019.

Variable	CG (n = 16)				PG (n = 18)					
	Baseline	Post	p-value	f2	Baseline	Post	p-value	f2	Post p-value*	f2
Self-esteem	30.50±6.60	33.13±4.30	0.26	0.21	30.44±5.12	35.11±3.84	0.011	0.85	0.170	0.02
Depressive symptoms	8.75±5.70	9.25±8.72	0.876	0.02	11.80±9.90	8.83±8.07	0.266	0.19	0.904	0.00

Note. f2 Cohen effect size. * p-value to comparison between CG and PG in the post intervention. Anova two-way with repeated measures and Sydak comparison test. CG – Control group. PG – Pilates group.

Table 3. Protocol analysis for self-esteem and depressive symptoms between Pilates method group and control group (n = 34). Florianopolis, SC – Brazil, 2019.

Variable	CG (n = 16)				PG (n = 11)					
	Baseline	Post	p-value	f2	Baseline	Post	p-value	f2	Post p-value*	f2
Self-esteem	30.50±6.60	32.07±3.90	0.566	0.14	29.25±5.22	34.70±3.60	0.013	1.08	0.860	0.07
Depressive symptoms	8.75±5.70	9.25±8.72	0.860	0.03	14.92±9.65	11.00±9.80	0.145	0.23	0.620	0.04

Note. f2 Cohen effect size. *p-value to comparison between CG and PG in the post intervention. Anova two-way with repeated measures and Sydak comparison test. CG – Control group. PG – Pilates group.

DISCUSSION

The present study aims to analyze the effects of 16 weeks of PG intervention in self-esteem and depressive symptoms in women with breast cancer undergoing hormone therapy. The results showed a relevant effect in self-esteem after the 16 weeks mat Pilates method intervention with a strong intervention size effect for this variable. However, it did not demonstrate significant results for depressive symptoms after the intervention.

The practice of adapted physical activity can help to improve self-esteem, quality of life and global health status in women with breast cancer²⁵, as shown in our results, when improvements in self-esteem were provided after the 16 weeks intervention with PG. These results may be contributed by fact the that the intervention took place in groups and all participants were in the same phase of treatment, it was a time when they talked about cancer and exchanged life experiences, providing affective bonds between them. Musanti²⁶ study also assessed self-esteem with the Rosenberg scale, similarly, found positive results from an exercise intervention among women with breast cancer. Moreover, the study from Bellver-Perez et al.27 showed evidence that group activities may enhance emotional states of women with breast cancer, as they provided some therapy interaction in groups. In addition, the presence of two health professionals during the classes always motivating the women may also have helped these results. Considering the findings, the social factor should gain attention during treatment in order to create interpersonal relationships that can contribute to the woman's process¹¹.

Improvements in self-esteem are very important for these women, as after mastectomy and breast-conservative surgery they demonstrated alterations in

psychological aspects, such as quality of life, self-esteem, and body image¹¹. Other study with 12 weeks of mat Pilates intervention also demonstrated an improvement on quality of life, mood, and body image¹². It is evident that 70.6% of participants of the present study did not undergo breast reconstruction. The breast is an organ that represents motherhood and female sexuality, that is why breast cancer compromises the female identity³, resulting in disorders in sexual and marital life during treatment, severely modifying their self-esteem. It is noteworthy that the Pilates protocol used in this study was efficient to improve the self-esteem of these participants.

According to Abreu et al.²⁸ the various changes that are caused by breast cancer directly affect the physical, psychological and rehabilitation status. In view of this, humanization during cancer treatment allows the creation of a closer and global relationship between the multidisciplinary team and the patient, finding solutions to problems that negatively impact quality of life. In addition, it enables the performance and development of therapy in a more humane way, considering the patient as an individualized person and with their own characteristics, whether physical and/or emotional, and improves the effectiveness of the treatment used.²⁹ The construction of a new form of care for users of health services based on humanization, takes into account that the user must have an integral and human approach. Therefore, their knowledge that is linked to their culture and that support their way of perceiving their own illness process must be respected³.

Given the physical damage caused by the treatment of breast cancer, there is evidence in the literature based on a systematic review by Pinto-Carral³⁰, that included four studies and demonstrated that Pilates method improves the health of this population, such as range of motion, pain and fatigue.

Developing postural improvements, reducing pain, makes them feel more motivated to move forward in the struggle for life, they obtain an improvement in their socialization and perception of their own body, learning to recognize it.^{3,11} The Pilates method was originally called "Control" which was based on Eastern theories of the spirit body, as there is a combined interaction with Western theories of motor learning and stability of the "spirit" center, emotionally encompassing the integration of mind-body welfare. This type of mind-body physical activity has shown good evidence for the benefits of women with breast cancer.

Another associated factor triggered during breast cancer treatment is depressive symptoms, which related to body image and self-esteem, may influence the quality of life of these women who suffered the consequences of treatment¹¹. The present study did not provide positive results regarding the change in depressive symptoms in both groups after the 16 weeks intervention, which may have happened because the women in the present study had a low baseline score for depressive symptoms.

Eyogor et al. ¹¹ study also using the BECK Inventory demonstrated significant positive results in depressive symptoms after eight weeks of intervention three times a week, differing from our results. This may have occurred because both groups walked twice a week for 20-30 minutes in addition to the Pilates intervention. Some studies that investigated interventions in women with breast cancer did not show significant results due to different factors, such as exercise

intensity, program adherence, body and mind interaction, and combination of physical abilities in the program ^{10-12,30}.

This study followed all protocol steps without any changes, demonstrating that the participants were able to perform all the exercises, proving to be a safe and effective non-pharmacological therapy to self-esteem in women during adjuvant hormone therapy for breast cancer treatment.

However, this study has some limitations that need to be clarified in order to properly interpret these findings, among them is the use of interview format questionnaire that leads to bias as it is not self-applicable; it was not possible to control the intensity of the exercises; another factor was the relatively small number of participants, since in Brazil the financial aid Ethics Committees are prohibited to collect data, unlike other countries, which may have limited the power in the study; and adherence of only 68% of the sessions.

CONCLUSION

The mat Pilates method proved to be a treatment option in improving the self-esteem of women with breast cancer undergoing hormonal therapy.

COMPLIANCE WITH ETHICAL STANDARDS

Funding

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Ethical approval

Ethical approval was obtained from the local Human Research Ethics Committee – CEPSH of UDESC and the protocol (no. 2.252.288) and by the Oncological Research Center Research Ethics Committee CEP protocol (no. 2.319.138) was written in accordance with the standards set by the Declaration of Helsinki.

Conflict of interest statement

The authors do not have any conflict of interests to declare.

Author Contributions

Conceived and designed the experiments: ACAG, LB, TBF. Performed the experiments: TBF. Analyzed the data: TBF. Contributed reagents/materials/analysis tools: LB, TBF, FS. Wrote the paper: ACAG, LS. Fretta TB, Boing L, Stein F, Santos L, Guimarães ACA.

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