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## Physical Activity During the Treatment of Women With Breast Cancer: A Systematic Review

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### ABSTRACT

Breast cancer incidence increases with age, and its treatment usually has side effects such as joint pain, depression and fatigue. Insufficient physical activity can decrease muscle strength, increase fatigue and reduce quality of life. Given the above, the purpose of this systematic review was to identify the main intervention strategies based on physical activities for women during breast cancer treatment. This study considered four databases: *PubMed*, *SportDiscus*, *Lilacs*, and *SciELO*, taking into consideration studies of the last five years. The descriptors for physical activity variable were "exercise", "physical activity", and "motor activity". For breast cancer variable, the descriptors were "breast neoplasm", and for participants: "women" and "adults". Seven studies related to the benefits of physical activity were found, one of those was carried out in Brazil. The variables studied were fatigue, anthropometry, physical activity level (PAL), pain threshold, sleep quality, life quality (LQ), physical fitness (PF), and cortisol level. The types of intervention strategies were in most part through aerobic exercises, resistance/strength training, hydrotherapy, relaxation, yoga and belly dancing. Although there is no consensus on which physical activity, intensity, and frequency are best for the patients, in general, all patients increased their level of physical activity and quality of life, reduced fatigue, and were not impeded by the treatment or found necessary to interrupt it while performing such physical activities.

**Keywords:** Breast cancer; physical activity; treatment; women.

### EXERCÍCIO FÍSICO DURANTE O TRATAMENTO DE MULHERES COM CÂNCER DE MAMA: UMA REVISÃO SISTEMÁTICA

### RESUMO

A incidência de câncer de mama aumenta com a idade e seu tratamento geralmente apresenta efeitos colaterais, como dor nas articulações, depressão e fadiga. Atividade física insuficiente pode diminuir a força muscular, aumentar a fadiga e reduzir a qualidade de vida. Diante do exposto, o objetivo desta revisão sistemática foi identificar as principais estratégias de intervenção com base na atividade física das mulheres durante o tratamento do câncer de mama. Este estudo levou em conta quatro bases de dados: *PubMed*, *SportDiscus*, *Lilacs* e *SciELO*, considerando estudos dos últimos cinco anos. Os descritores para a variável atividade física foram "exercise", "physical activity", e "motor activity". Para a variável câncer de mama, os descritores foram "breast neoplasm", e para as participantes: "women" e "adults". Entre sete estudos relacionados aos benefícios da atividade física, um deles foi realizado no Brasil, cujas variáveis foram fadiga, antropometria, nível de atividade física (NAF), limiar de dor, qualidade do sono, qualidade de vida (QV), aptidão física (AP), nível de colesterol. Os tipos de estratégias de intervenção foram, em grande parte, por meio de exercícios aeróbicos, treinamento de força/resistência, hidroterapia, relaxamento, yoga e dança do ventre. Embora não haja consenso sobre qual atividade física, intensidade e frequência são melhores às pacientes, em geral todas elas aumentaram o nível de atividade física e qualidade de vida, reduziram a fadiga e não foram impedidas pelo tratamento ou acharam necessário interrompê-lo durante a realização de tais atividades físicas.

Palavras-chave: Câncer de mama; atividade física; tratamento; mulheres.

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## INTRODUCTION

Breast cancer is characterized by abnormal cell multiplication forming nodules or tumors that may develop slowly or rapidly. It can be caused by environmental and behavioral factors, reproductive background, and hormonal, genetic and hereditary factors. It is estimated that 59,700 new cases will occur in Brazil for each year of the two-year period of 2018-2019, with an approximate risk of 56.33 cases every 100 thousand women.<sup>1</sup>

The incidence of breast cancer increases with age. 95% of the cases occur from 40 years old, however, while the cancer rate in women of more than 50 years old remained stable between 2005-2014, the cancer rate in women of less than 40 years old increased 0.2% a year since the 90s.<sup>2</sup>

One of the main concerns about breast cancer is that it affects a body organ that represents one of the symbols of the female universe.<sup>3</sup> Studies on mastectomized women due to breast cancer showed a change in their body self-image due to the treatment's aggressiveness.<sup>4</sup> The treatment also influenced the modification on the sexual identification and marital relationship.<sup>5,6</sup> Women that undergo breast cancer treatment present many reactions, such as: undermined general well-being, joint pain, depression and fatigue.<sup>7,8</sup> Then, it is common that patients feel discouraged to practice physical activities (PA).<sup>9</sup> Insufficient physical activity and the consequent decrease of muscle strength,<sup>10</sup> can be a predictor of fatigue persistence in breast cancer survivors.<sup>11</sup> Healthy habits, such as the customary practice of physical activity (HPPA), healthy eating, breast feeding and low alcohol and cigarettes consumption can prevent up to 30% of breast cancer cases.<sup>1</sup>

However, some studies already have some reports on the improved quality of life and decreased mortality rates in breast cancer patients.<sup>10,12</sup> Such studies are related to the fact that some patients, when receiving the cancer diagnosis, adopt a healthier lifestyle, increasing their consumption of fruits and vegetables, abstinence from cigarettes and alcohol, and frequent physical activity.<sup>12</sup>

Studies<sup>13-14, 9</sup> had different approaches on the application of physical activities during breast cancer treatment, however, there is no consensus on the amount, intensity and duration in order for these activities to be more beneficial to this population.<sup>15</sup> Recently, women with breast cancer were subject to group physical activity intervention, which resulted in significant life quality (LQ) improvement when comparing to custom intervention.<sup>16</sup> In view of the above, the purpose of this study is to review systematically the main physical activities-based intervention strategies for women during breast cancer treatment.

## METHODS

This study is a systematic review of the literature from articles published between 2013-2017, the search for the material was carried out in September 2018 – December 2018, considering as dependent variable: breast cancer, and independent variable: physical activity.



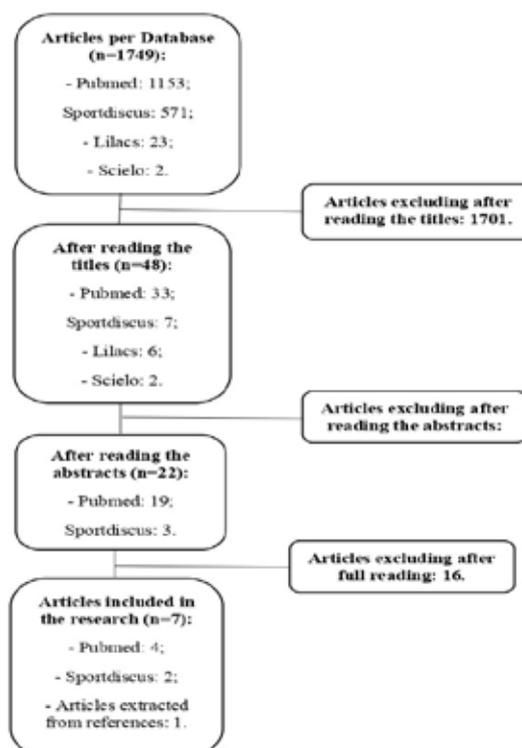
This research included clinical intervention studies performed on women with breast cancer of ages above 19 years old, in English and Portuguese, using four databases: *PubMed*, *SportDiscus*, *Lilacs*, and *SciELO*. Three researchers conducted this research independently. The descriptors used for the physical activity variable were “*exercício*”, “*atividade física*”, “*aptidão física*”, “*atividade motora*”, in Portuguese, and “*exercise*”, “*physical activity*” and “*motor activity*”, as the corresponding descriptors in English. For the breast cancer variable, the descriptor used was “*breast neoplasm*”. For research participants, the descriptors used were “*women*” and “*adults*”.

The analysis process had four phases: reading of the titles, abstracts, and articles in full, and references extraction. At the end of each phase, a meeting would take place to define the inclusion or exclusion of each article. In the event of disagreement between three researchers, two researchers would reach a consensus to decide on whether the article would be included or not in the research.

At the end of the searches on the databases,  $n=1749$  studies were found, of which 1701 were excluded after the reading of the titles (1120 *Pubmed*, 564 *Sportdiscus*, and 17 *Lilacs*), and, after the reading of the abstracts 26 were excluded (14 *Pubmed*, 4 *Sportdiscus*, 6 *Lilacs*, 2 *Scielo*) remaining 22 articles to be read in full. After the full reading phase, 6 articles remained (4 *Pubmed* and 2 *Sportdiscus*). Moreover, another article was added with basis on the references for having quotes on resistance training intervention with women under radiotherapy treatment in one of the studies used in the introduction of this paper, totaling 7 studies considered for the analysis (Image 1).



Image 1 – Flow-chart of the systematic review phases



Source: Prepared by the authors.

## RESULTS

From the seven studies selected (Table 1), four were carried out in the European Continent,<sup>9,13,17-18</sup> two in the United States,<sup>14,19</sup> and one in Brazil,<sup>7</sup> The age average of the participants was 51.6 years old. A large variation in sample size was observed in the studies found, with the smallest being n=22, divided between intervention and control.<sup>7</sup> The highest number of participants was n=163, also divided between intervention and control.<sup>19</sup>

The studies selected analyzed the interference of physical activity on different variables: PAL,<sup>7, 9,13-14</sup> LQ,<sup>7,13-14,18-19</sup> fatigue,<sup>7, 9, 13-14, 17-18</sup> anxiety,<sup>7,13,18-19</sup> pain threshold,<sup>17</sup> sleep,<sup>19</sup> PF,<sup>9,13-14</sup> anthropometry<sup>17</sup> and cortisol,<sup>19</sup> The methodological quality of the selected studies was assessed using the score obtained from the PEDro database.<sup>20</sup> One study<sup>7</sup> was not indexed to the database (Table 1).

Table 1 – Main features of the studies according to age, sample, country and variables studied

Author/year	Age (average in years)	Sample size	Country	Study Variables	PEDro scale
Husebo et al. (2014) <sup>9</sup>	52,2	67 (33 intervention and 34 control)	Norway	Fatigue, PAL and PF	6/10
Cornette et al. (2016) <sup>13</sup>	50,5	44 (22 intervention and 22 control)	France	PF, LQ, PAL, Fatigue, Anxiety and Depression	5/10
Boing et al. (2017) <sup>7</sup>	54,1	22 (11 intervention and 11 control)	Brazil	LQ, Fatigue, Depression e PAL	NA
Chandwani et al. (2014) <sup>19</sup>	51,8	163 (109 intervention and 54 control)	United States	QV, Depression, Sleep, and Cortisol Level	4/10
Cantarero-Villanueva et al. (2013) <sup>17</sup>	47,3	40 (20 intervention and 20 control)	Spain	Pain threshold, Fatigue and Anthropometry	4/10
Ligibel et al. (2016) <sup>14</sup>	50	98 (47 intervention and 51 control)	United States	QV, PAL, Fatigue, AP	6/10
Steindorf et al. (2014) <sup>18</sup>	55,8	155 (77 intervention and 78 control)	German	Fatigue, QV, Depression	7/10

Legend: PAL (Physical Activity Level); PF (Physical Fitness); LQ (Life Quality); NA (not applicable for no indexation to the database PEDro).

Source: Prepared by the authors.

To assess LQ, four studies used the questionnaire from the European Organization for Research and Treatment of Cancer (EORTC),<sup>7,13-14,18</sup> and one study used the Medical Outcomes Study 36-item short-form survey (SF-36).<sup>19</sup> Fatigue was assessed by six studies through different questionnaires: Brief Fatigue Inven-



tory,<sup>19</sup> Multidimensional Fatigue Inventory (MFI-20);<sup>13</sup> Piper Fatigue Scale<sup>7,17</sup> and Functional Assessment of Chronic Illness Therapy (FACIT)<sup>7,14</sup>.

Table 2 – Qualitative analysis of types of intervention, results and conclusions on the studies included

Author/Year	Intervention	Statistics	Results	Conclusion
Husebo et al. (2014) <sup>9</sup>	30' daily walk + strength training for 18 weeks – 3x/week (telephone monitoring).	Descriptive statistics, ANOVA one-way and ANOVA mixed.	↑ Fatigue after intervention; ↑ PAL and PF 6 months after = intervention on both groups. There was no difference between the groups.	There was no improvement on Fatigue, PAL e PF. However, physical activity seemed applicable.
Cornette et al. (2016) <sup>13</sup>	20' – 40' aerobic activity 2x/week + strength training 1x/week for 27 weeks (telephone monitoring).	Independent test t, Mann-Whitney and ANOVA for repeated measures.	↑ Aerobic and functional capacities in the intervention group. There was no difference between the groups.	There was no PF improvement between the groups. However, the activity seemed applicable.
Boing et al. (2017) <sup>7</sup>	60' of belly dancing 2x/week for 12 weeks.	Fisher's and ANOVA's exact test	↑ QV e ↓ Fatigue and depression in the intervention group. There was no difference between the groups.	Belly dancing influenced the patient's LQ.
Chandwani et al. (2014) <sup>19</sup>	60' stretching or yoga 3x/week for 6 weeks.	Regression analysis and mixed models.	↑ LQ with yoga; ↓ Fatigue in all groups; no difference in sleep; ↓ cortisol with yoga.	Intervention with yoga showed better results in the population studied.
Cantarero-Villanueva et al. (2013) <sup>17</sup>	60' hydrotherapy 3x/week for 8 weeks.	Independent t Test, ANOVA one-way, chi-squared and ANCOVA test	↑ of pain threshold; ↓ anthropometry; Fatigue had no difference between groups.	Intervention with hydrotherapy showed positive results and seemed applicable for the population.
Ligibel et al. (2016) <sup>14</sup>	150'/week of AFMV for 16 weeks (telephone monitoring).	Wilcoxon and Fisher's exact test	↑ PF, no difference to LQ and PF.	Intervention was applicable, but ineffective to differentiate the groups.
Steindorf et al. (2014) <sup>18</sup>	60' resistance training and relaxing 2x/weeks for 12 weeks.	Covariance Analysis Model for individual changes (ANCOVA)	↓ Fatigue in the resistance-training group. There were differences between groups.	Intervention physical activity improved fatigue more than relaxing.

Legend: ↑(increase) ↓(reduction) PAL (physical activity level); PF (Physical Fitness); LQ (Life Quality); MPA (Moderate Physical Activity).

Source: Prepared by the authors.

For PAL assessment, three studies used the International Physical Activity Questionnaire IPAQ.<sup>7, 9,13-14</sup> All studies showed increase in physical activity level, but the information was collected indirectly in one of the studies, through telephone interview.<sup>14</sup> Physical fitness was assessed pursuant to the patient's health condition. In two studies,<sup>9,13</sup> physical fitness was assessed with a six-minute walking test. In another study,<sup>14</sup> with patients with metastases, this assessment was



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made by modified Bruce protocol. To measure the maximum oxygen volume (max  $\text{VO}_2$ ) the Cardiopulmonary Exercise Test (CPET) was used.<sup>13</sup>

Moreover, sleep quality was assessed through the *Pittsburgh Sleep Quality Index (PSQI)* questionnaire,<sup>19</sup> as well as depression, which also was assessed by the Center for Epidemiological Studies-Depression CES-D score.<sup>18-19</sup> Anxiety and depression were assessed together by the *Hospital Anxiety and Depression (HADS)*<sup>13</sup> and depression through *BECK's Depression Inventory (BECK)* questionnaire.<sup>7</sup> Cortisol levels were assessed through saliva collection after physical activity,<sup>19</sup> and pain threshold through pressure by algometer in specific parts of the body.<sup>17</sup>

Consequently, we observed a heterogeneity in the types of intervention applied in the studies (Table 2). Two studies applied essentially aerobic interventions,<sup>14,17</sup> one study used intervention through resistance training,<sup>18</sup> two applied aerobic and strength exercises combined,<sup>9,13</sup> one applied yoga classes,<sup>19</sup> and another one applied belly dancing classes.<sup>7</sup>

The study carried out with telephone monitoring with instructions on how to perform aerobic and strength exercises for 18 weeks showed fatigue increase, however, PF and PAL improved. There was no difference between the groups.<sup>9</sup> In another study of combined intervention that lasted 27 weeks, there was an increase in the functional and aerobic capacity, but with no differences between groups.<sup>13</sup> On the other hand, in the study that compared the resistance training with relaxation, performed 2 times a week for 12 weeks, there was a fatigue decrease in the resistance training group with difference between the groups.<sup>18</sup>

The application of water activities for 60 minutes, 3 times a week, identified increase of pain threshold, reduction of the abdominal circumference and fatigue reduction, but there was no differences between groups<sup>17</sup>. Yoga or stretching intervention practiced for 6 weeks, for 60 minutes, 3 times a week, managed to reduce fatigue and improve sleep, specially yoga that improved fatigue and LQ, when compared to stretching<sup>19</sup>. Belly dancing, during 12 weeks, with duration of 60 minutes, 2 times a week, increased life quality and reduced fatigue and depression, although there were no differences between groups.<sup>7</sup>

## DISCUSSION

The finding of the studies suggest that aerobic physical activity and resistance training can be used as a supporting option helping women with their cancer treatment. Moreover, save the proper care with exercises for the lower limbs, Yoga and Belly Dancing also proved applicable. As to the intensity, there is no consensus, but the majority of studies use moderate intensity, having as reference the max.  $\text{VO}_2$  or heart rate.

Fatigue was the most relevant variable in the studies found, since it is one of the main symptoms and side effects of breast cancer treatment.<sup>7,9,18</sup> Fatigue is attributed to the chemotherapy cardiotoxicity and its prevalence occurs in 80-90% of cancer patients, who usually present left ventricular systolic dysfunctions.<sup>21</sup> With regards to the results found, only the study using resistance training



showed differences between the control and intervention group,<sup>18</sup> however, everyone presented an improvement in fatigue level after the interventions.

In addition to fatigue, another relevant factor identified in the studies was the pain threshold<sup>17</sup>, increase after water activities intervention, which can also be a LQ improvement factor. However, the authors warn that it is not possible to know specifically if these benefits were only achieved with the intervention of water exercise, given the beneficial hydrostatic effects of water itself. In addition, the use of warm water might have influenced the nociceptor (pain) peripheral stimulating receptors, which may have contributed to the increase of pain threshold.

In this sense, the two hypothesis for the reasons that may have contributed for the lack of differences statistically significant between most interventions were the monitoring form and PAL assessment. In three studies<sup>9,13-14</sup> the monitoring method, both of the intervention and control group, was performed through the telephone. The aerobic activities were, respectively: 30-minute walk, 3 times a week, for 18 weeks; 20-40 minutes of non-specific aerobic activity (walk or cycle ergometer) 2 times a week + strength training 1 time a week, during 27 weeks; and 150 minutes of moderate walking for a week, during 16 weeks. This condition makes difficult to monitor the systematized practice of physical activity. In relation to PAL assessment, even though the IPAQ has been used in four studies,<sup>7,9,13-14</sup> in one of them.<sup>14</sup> With patients with metastatic cancer and many types of treatment (hormonal, biological and chemotherapy) the IPAQ assessment was through the telephone, which may have contributed to the subjectivity of the method.

However, the studies selected indicate the decrease of the participants' sedentary behaviors since the beginning of the interventions up to the last assessment, which shows the possibility of a positive conclusion that physical activity can have on the increase of the physical activity level of patients with cancer. In addition to the fact that there was no report on the patients' impediment or need to interrupt the exercises.

The studies included in this paper indicate that LQ is directly related to high fatigue levels, anxiety, depression and stress, however, in one of these studies,<sup>19</sup> the use of yoga as a physical activity managed to reduce fatigue and cortisol levels of the participants, increasing LQ levels. In this study, only the sleep variable did not present relevant difference that could contribute to LQ improvement. On the other hand, in another study,<sup>14</sup> the participants reported good LQ perception in the baseline, i.e., before the intervention, this data may have affected the results after the intervention, since LQ in this study did not show relevant differences.

Interventions with onsite monitoring,<sup>7,17,19</sup> both individually (resistance training) and in group (Yoga, belly dancing) showed better results in fatigue, depression and LQ when compared to those performed through telephone monitoring.<sup>9, 13-14</sup>

Recruitment and randomization could also have contributed as a potential bias for the differences not being relevant in the interventions, in their majority.



In the study on resistance training,<sup>18</sup> the only to present relevant differences in fatigue, the patients were invited to participate of the intervention physical activity since their first day of radiotherapy. Physical education teachers and physical therapists monitored those patients at a gym attached to the hospital and radiotherapy service. We can infer that the systematization of physical activity and greater monitoring control by professionals from specific areas, respectively, may have contributed for this positive difference as the resistance training has indicated.

Studies with post-treatment physical activities were not investigated. Thus, future studies must consider the need for objectively monitoring control groups, and new studies must consider specific groups of women under breast cancer treatment, such as, for example, stratify chemotherapy, radiotherapy or hormone therapy treatments, including the specific stages of the disease.

## CONCLUSION

Although this review does not identify a pattern on which type of physical activity is more recommended for patients under breast cancer treatment, there was no complication that prevented the patients from practicing the physical activities proposed. In general, all patients showed positive results in relation to the variables studied, evidencing the importance of physical activity in this population. Future studies must be developed to clarify the intensity and frequency necessary to reach better LQ levels during cancer treatment.



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