

Fatigue and depression improvements on breast cancer survivors practitioners of strength training

Melhorias na fadiga e na depressão em sobreviventes de câncer de mama praticantes de treinamento de força

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Abstract – Due to the high incidence of breast cancer worldwide, it is important to research and understand the physiological and psychological effects of this disease, like fatigue, depression, and capacity to do daily life tasks and how they modify physical activity. This study aimed to analyze the effects of strength training practice on physical fatigue (IMF-20), depression (Beck questionnaire), handgrip strength, and functional performance (time up and go). The sample was composed of 17 women breast cancer survivors, in which 8 volunteers were strength training practitioners for at least 6 months (P), and 9 volunteers were non-practitioners (NP). The T-test identified significant differences ($p > 0.05$) between groups on fatigue ($P = 7.37 \pm 1.76$; $NP = 10.77 \pm 3.41$; $p = 0.02$) and depression ($P = 8.75 \pm 5.20$; $NP = 14.55 \pm 4.21$). There was no significant difference between groups on handgrip strength and functional performance.

Key words: Breast neoplasms; Physical activity; Case-control study; Rehabilitation; Resistance training.

Resumo – Devido à alta incidência de câncer de mama em todo o mundo, é importante pesquisar e entender os efeitos fisiológicos e psicológicos dessa doença, como fadiga, depressão e capacidade de realizar tarefas da vida diária e como elas se modificam com a atividade física. O objetivo deste estudo foi analisar os efeitos do treinamento de força na fadiga física (IMF-20), depressão (questionário de Beck), força de preensão manual e desempenho funcional (timed up and go). A amostra foi composta por 17 mulheres sobreviventes de câncer de mama, das quais 8 voluntárias eram praticantes de treinamento de força há pelo menos 6 meses (P) e 9 voluntárias eram não-praticantes (NP). O teste T identificou diferenças significativas ($p > 0,05$) entre os grupos sobre fadiga ($P = 7,37 \pm 1,76$; $NP = 10,77 \pm 3,41$; $p = 0,02$) e sobre depressão ($P = 8,75 \pm 5,20$; $NP = 14,55 \pm 4,21$). Não houve diferença significativa entre os grupos em força de preensão manual e desempenho funcional.

Palavras-chave: Neoplasia da mama; Atividade física; Estudo caso-controle, Reabilitação; Treinamento resistido.

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INTRODUCTION

Breast cancer (BC) is the most common malignant neoplasm in women¹. The BC is characterized by cells disordered growth and multiplication in breast tissues, formed cellular clusters called tumors². In 2018, approximately 2.1 million new cases of BC were diagnosed worldwide, and according to the INCA, the BC is the main responsible for deaths of women due to cancer globally³.

Significant improvements in detection and treatment caused an increase in patients' survival rate; however, both the pathology and the treatment may trigger side effects directly proportional to the disease severity and the intervention⁴⁻⁶. In this sense, breast cancer survivors (BCS) tend to present neuroendocrine, physiological, and psychological changes. These metabolic changes are associated with fatigue, reduced strength and muscle mass, loss of physical functionality, depression, and consequently the quality of life loss⁷⁻⁹.

Several studies have demonstrated a decrease in BCS physical function and quality of life after starting treatment¹⁰⁻¹². Simonavice et al.¹⁰ noted that BCS who underwent the first treatment 17 months ago have muscle strength loss, 21% in the chest press and 23% in the leg extension when compared to healthy and sedentary women matched by age. These physical dysfunctions are associated with psychological changes and can lead to depression. Thus, the development of alternative therapies, such as non-pharmacological treatments is necessary to mitigate the side effects of disease and treatment, in addition to promote a better quality of life for this population¹⁰.

To alleviate late side effects, reduce fatigue and prevent the loss of skeletal muscle tissue, authors have proposed strength training (ST) as a safe and effective intervention¹³⁻¹⁵. ST reduces fatigue, improves cardiovascular functions, and increases skeletal muscle tissue and protein synthesis, in addition to gains in strength and physical function.

The American College of Sports Medicine¹⁶ recommends ST for cancer survivors who have already completed treatment at a frequency of two or three times a week. BCS that follow the recommendations shows good adherence to the intervention with ST and improvement in physical function when performed at moderate intensities¹⁰.

In this sense, the study aims to investigate the importance of ST practicing after BC treatment, characterizing and comparing transversal data of functional performance, handgrip strength, fatigue, and depression between 2 BCS groups, both with similar cancer treatments, but different in practicing or non-practicing of ST. The results obtained in this comparison may help health professionals to decide the appropriate intervention after BC treatment, and the possibility to include ST practicing for BCS for physical conditioning and quality of life.

METHODS

SAMPLE

The sample consisted of 17 BCS women diagnosed with BC in stages I to IIIC, who completed radiotherapy or chemotherapy treatments at least six months ago. Also, some participants participated in a strength training program

twice a week. Furthermore, data were conducted as soon as they completed six months of training. Survivors who had a diagnosis of cancer-related lymphedema, cardiovascular changes, metabolic or osteomyoarticular limitations, or who had secondary neoplasms and metastasis were not included.

All volunteers were informed about the objectives, procedures, possible risks, as well as the study benefits, and they were only included in the experimental procedures after signing the Consent Form. This study was approved by the Ethics and Research Committee of the University Center of Brasília (CAAE 86773918.0.0000.0023).

STUDY DESIGN

This is a case-control study. Participants were selected from public and private hospitals, of which 8 volunteers were previously practicing strength training regularly in the last 6 months, the group of practitioners (P), and 9 non-practitioners (NP) volunteers. The protocol was conducted at the Faculty of Physical Education at the University of Brasília and the participants attended one day for all the procedures. The tests performed were conducted in the following sequence: a) Anamnesis b) Fatigue Questionnaire c) Depression Questionnaire d) Anthropometric assessments e) Handgrip Strength f) Time Up and Go (TUG).

ANAMNESIS

Questionnaires were applied to characterize the sample with data regarding age, diagnosis time, treatment type, treatment time, and physical activity level. Also, data were obtained regarding possible side effects before and after disease diagnosis, as well as during treatment.

FATIGUE QUESTIONNAIRE

Fatigue was assessed by the Inventory Multidimensional Fatigue (IMF-20). The IMF-20 was designed to assess different levels of fatigue between individuals, groups, or different conditions, and can be applied to different populations. The questionnaire contains 20 items that relate to five dimensions of fatigue experienced during the previous days: 1 - General fatigue; 2 - Physical fatigue; 3 - Mental fatigue; 4 - Activity reduction; 5 - Motivation reduction. The score is calculated for each dimension and the values vary from 4 to 20 in a direct proportion to the fatigue degree. In the present study, we used physical fatigue as perceived fatigue¹⁷.

DEPRESSION QUESTIONNAIRE

To assess depression, we used the Beck questionnaire. Beck's depression inventory is a self-report scale to collect data on the intensity of depressive symptoms. The scale has 21 items, each item is assessed on a 4-point scale, in the end, and all points obtained are added up and give a score ranging from 0 to 63 points. Scores are classified as follows: 0 to 13-no depression; 14 to 19-mild

depression; 20 to 28-moderate depression; 29 to 63-severe depression¹⁸. The questionnaires were provided to the patients by a graduate psychologist, and the same collaborator analyzed these data.

ANTHROPOMETRIC ASSESSMENTS

The height was measured using a stadiometer with a precision of 0.1 cm, from the Sanny brand, Professional Sanny model (measuring range from 40 cm to 210 cm). Body mass was measured by a digital scale with a capacity of 200 kg and a resolution of 50 g, of the Ramuza brand, model ISR 10,000. The determination of the body mass index (BMI) was calculated by the ratio between mass and height squared.

HANDGRIP STRENGTH

Handgrip strength (HGS) was measured with a Jamar[®] hydraulic hand dynamometer (Sammons Preston, Illinois, USA) according to the American Society of Hand Therapists recommendations¹⁹. The measurements were performed with the participants in a seated position, elbow at 90°, forearm in a neutral position, and wrist between 0° and 30° in extension. The average of three attempts in the right and left hands was used for analysis.

TIME UP AND GO

Functional performance was assessed using the Time Up and Go (TUG) test. The protocol consists of getting up from a chair, walking 3 linear meters to a visible mark made on the floor, turning around the mark, walking back to the chair, and sitting down again at the shortest possible time. The chair was standardized at a height of 46 cm and when the researcher signaled, the time started to count. The count was finished as soon as the volunteer returned and sat down completely. Three attempts were performed with a 60 seconds interval between series, the shortest time between the three attempts was used to quantify the functional performance²⁰.

STATISTICAL ANALYSES

The normality of the data was verified by the Shapiro-Wilk test and the variables showed normal distribution the parametric tests were selected. The independent T-test was used to compare groups (P x NP). The level of statistical significance adopted was 5% ($p \leq 0.05$). All analyzes were performed using SPSS statistical software version 21 (SPSS Inc., Chicago, IL, USA).

RESULTS

The data were expressed as means and standard deviations. The descriptive and comparative data of the P and NP are shown in Table 1. No significant differences were found in physical characteristics and types of treatment.

Table 1. Descriptive data and comparatives of P and NP, expressed in mean and \pm standard deviation.

	P (n=8)	NP (n=9)	p
Age (years)	51.12 \pm 4.64	50.33 \pm 8.50	0.201
Height (m)	1.61 \pm 0.065	1.61 \pm 0.066	0.555
Weight (kg)	73.39 \pm 11.085	77.98 \pm 20.522	0.219
BMI (kg/m²)	28.218 \pm 4.62	29.95 \pm 7.38	0.200
QT	11.67 \pm 4.08	9.63 \pm 4.27	0.719
RT	23.20 \pm 8.75	24.50 \pm 11.735	0.545
Staging			
IA	0%	11.1%	
IB	25%	33.3%	
IIA	0%	33.3%	
IIB	25%	22.2%	
IIIA	12.5%	0%	
IIIB	25%	0%	
IV	12.5%	0%	

Note. P: Practitioners Group; NP: Non-Practitioners Group; BMI: Body Mass Index; QT: Quantity of chemotherapy sessions; RT: Quantity of radiotherapy sessions. IA, IB, IIA, IIB, IIIA, IIIB and IV describe, in this order, the severity of cancer stages diagnosed by a doctor. The early stages are characterized by smaller tumor measures and no lymph nodes (axillar and breastbone) involvement. According to the increase of tumor size and lymph nodes cancer (size and quantity), the BC is anchored by more advanced stages. In the latest phases, the tumor may spread to the chest wall or the skin, until spreading to other organs of the body. When this occurs, it is described as metastatic cancer, the later stage.

Table 2 shows physical fatigue, depression, handgrip strength, and TUG scores in both groups. There are significant differences in physical fatigue and depression between the groups, where the T value was significantly lower ($p = 0.02$).

Table 2. Variables of self-reported fatigue, handgrip strength, and time up and go expressed in mean and \pm standard deviation.

	P (n=8)	NP (n=9)	p
Physical Fatigue	7.37 \pm 1.76*	10.77 \pm 3.41	0.02
Depression	8.75 \pm 5.20*	14.55 \pm 4.21	0.02
HGS-Right (KGf)	20.0 \pm 3.70	19.11 \pm 3.62	0.62
HGS-Left (KGf)	17.0 \pm 3.42	18.44 \pm 0.43	0.51
Time Up and Go (seconds)	5.75 \pm 5.89	5.21 \pm 0.44	0.49

Note. *Significative difference in relation to NP ($p < 0.05$).

DISCUSSION

The present study investigated whether BCS practitioners of ST had functional performance, handgrip strength, perceived fatigue, and depression levels better than non-practitioners. The main results showed that BCS practitioners of ST for 6 months have less perceived physical fatigue and depression than the non-practitioners group. However, no differences were found in functional performance (TUG), handgrip strength, and general fatigue.

Effects such as decreased strength, quality of life, persistent fatigue, and depression are commonly reported by cancer survivors even after treatment^{5,10,21}. Several studies have demonstrated the efficiency of ST in the systemic changes control, such as inflammatory, metabolic, and hormonal disruptions, caused by the disease and treatment²²⁻²⁴. Such factors may explain the lower rates of physical fatigue and depression in the P group.

Fatigue is the most reported side effect of BCS even after treatment²⁵. A range of common problems is associated with cancer in women with BC. The

most related are treatment side effects, obesity, sleep disturbances, psychological effects, and comorbid conditions. The lower fatigue found in the P group is possibly related to these factors, despite these variables were not analyzed, some studies have shown that physical activity helps to regulate sleep, mood, and variation of cortisol⁹.

The key mechanism of cancer-related fatigue is inflammation. Fatigue and inflammatory processes may also be influenced by psychological, behavioral, neuroendocrine dysregulation, immune and mitochondrial dysfunction. Proinflammatory cytokines (IL-1 β , TNF- α , and IL-6) may be released by the tumor, signaling to the central nervous system, leading to physical fatigue and other behavioral changes. These alterations may contribute to persistent inflammation and associated symptoms of fatigue²⁶. Physical exercise stimulates mitochondrial biogenesis and is an effective strategy for treating cancer-related fatigue and may act through several pathways, including a decrease in serum proinflammatory cytokines⁸.

When the fatigue effects persist after treatment, there is a reduction in activities of daily living and an increase in exposure to other comorbidities associated with a sedentary lifestyle. On the other hand, physical inactivity contributes to fatigue persistence and other side effects, causing a vicious cycle of events that complement each other, however, this bad cycle can be interrupted with the physical exercise practice²⁴.

Also, when comparing the P with the NP groups, our study indicated that ST can be a good strategy for controlling depression ($p < 0.02$). Depression affects more than 10% of BCS, which is usually related to emotional stress caused by the diagnosis, but it is also associated with pain caused by treatment, fatigue, reduced daily activities, and physical disability. In addition to the emotional and psychosocial dimensions of depression in cancer, inflammatory mechanisms seem to be important. Tissue destruction leads to the production of numerous pro-inflammatory cytokines. Many of these cytokines have also been observed to increase the activity and expression of serotonin and noradrenaline reuptake transporters. Furthermore, these cytokines reduce levels of brain-derived neurotrophic factor (BDNF), which is a key factor for neurogenesis. Lower levels of BDNF and neurogenesis have been implicated in the pathogenesis of depression^{2,27}. The lower level of depression found in the P group is possibly related to the regulation of these parameters. Although these variables were not analyzed, some studies have shown that physical activity regulates proinflammatory cytokines⁸ and stimulates BDNF²⁸.

Some conventional treatments for depression may be contraindicated depending on the type of cancer and cancer treatment. The use of ST, as a non-drug intervention, has been proposed to control side effects (fatigue, pain, and physical disability) associated with depression^{2,29}. These factors corroborate the findings of the present study, which suggest that ST is capable of reducing depressive symptoms of BCS, as shown in other studies³⁰.

Despite all the systemic benefits generated by ST, there was no significant difference in HGS and functional performance for BCS. These results may have occurred due to the lack of specific exercises for the development of these variables, such as exercises for the forearm and hand muscles, and exercises for functional performance.

Although our study presents important results, there are limitations regarding the low sample size. Therefore, our results reinforce other studies which found

great results in favor of the benefits of ST in BCS^{11,16,23}, and other studies show that ST may be beneficial for BC patients^{15,24,25}. These results should be considered preliminary and future prospective studies are recommended to confirm our findings. Another possible limitation of this study is the absence of data about education level, economic status, time after surgery, by the possibility of a direct or indirect influence in the fatigue or depression levels. Although, we had cautioned in the sample chase, being cautelous of choosing BCS at least 6 months after surgery. The T-test didn't reject the null hypothesis of chemotherapy or radiotherapy number of sessions between groups. Unfortunately, social data were not assessed by the questionnaires.

Further studies with a bigger sample and more time of ST practicing are needed to find possible differences in handgrip strength and functional performance. Health professionals may encourage breast cancer survivors to exercise to improve their quality of life.

CONCLUSION

BCS practitioners of ST have better rates of depression and physical fatigue than non-practitioners BCS. And as the unique treatment point that differs in the two groups is the practice of ST, it allows us to conclude that there is a high probability of training contribution in this improvement. By the way, other factors that could confuse this interpretation, like the type of treatment, number of treatment sessions and prior cancer stage are not different between groups. Health professionals may encourage physical exercise for BCS to improve their quality of life by reducing fatigue levels and depression scores.

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COMPLIANCE WITH ETHICAL STANDARDS

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Ethical approval

Ethical approval was obtained from the Ethics and Research Committee of the University Center of Brasília (CAAE 86773918.0.0000.0023).

Conflict of interest statement

The authors declare that they have no competing interests.

Author Contributions

Conception and design of the experiment: SNC, FDL, BBP, JV, JME, LAR, AKSS, SC, RJO. Realization of the experiments: SNC, FDL, BBP, JV, JME, LAR, AKSS, SC, RJO. Data analysis: SNC, FDL, BBP, JV, JME, LAR, AKSS, SC, RJO. Contribution with reagents/research materials/analysis tools: SNC, FDL, BBP, JV, JME, LAR, AKSS, SC, RJO. Article Writing: SNC, FDL, BBP, JV, JME, LAR, AKSS, SC, RJO. All authors read and approved the final version of the manuscript.

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