

Effect of a Physical Exercise Program on Acute and Chronic Blood Pressure in Breast Cancer Survivors

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Efeito de um Programa de Exercício Físico na Pressão Arterial Aguda e Crônica em Sobreviventes de Câncer de Mama
Efecto de un Programa de Ejercicio Físico sobre la Presión Arterial Aguda y Crónica en Supervivientes de Câncer de Mama

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ABSTRACT

Introduction: Few studies have explored the outcome of hemodynamic components in cancer survivors in a physical exercise programs. **Objective:** The main objective of this study was to verify acute and chronic changes in systolic (SBP) and diastolic (DBP) blood pressure during an exercise program for breast cancer survivors. **Method:** In a referral hospital, 24 surviving women participated in a physical exercise program. The BP was monitored with a digital wrist monitor, before and after the sessions. For pre and post-exercise comparison in each session, the *t* test for paired samples was used. For analysis of chronic effects, analysis of variance (ANOVA) was used, with repeated measures to identify possible differences in pre-exercise variables SBP and DBP throughout the 15 sessions. The level of significance was 5%. **Results:** It was noticed that, with the exception of the fourth and sixth sessions, the SBP levels decreased in all sessions after exercise ($p \leq 0.05$). For DBP, there was only a significant decrease after exercise in the first three sessions. For chronic effects, there was an average reduction in the values of SBP at rest throughout the sessions, with a hypotensive effect above 70% from the seventh session ($p \leq 0.05$). In DBP, differences in SBP values at rest were accentuated after the tenth session; when comparing with the values of DBP at rest, a hypotensive effect above 94% was observed. **Conclusion:** Survivors who adhered to the physical exercise program showed acute and chronic reduction in SBP and DBP.

Key words: cancer survivors; arterial pressure; exercise.

RESUMO

Introdução: Poucos estudos exploraram o desfecho de componentes hemodinâmicos em sobreviventes de câncer em um programa de exercícios físicos. **Objetivo:** Verificar alterações agudas e crônicas na pressão arterial sistólica (PAS) e diastólica (PAD) durante um programa de exercícios em sobreviventes de câncer de mama. **Método:** Em um hospital de referência, 24 mulheres sobreviventes participaram de um programa de exercícios físicos. A PA foi monitorada com monitor digital de pulso, antes e após a realização das sessões. Para comparação pré e pós-exercício em cada sessão, foi empregado o teste *t* para amostras pareadas. Para análises dos efeitos crônicos, utilizou-se a análise de variância (Anova), com medidas repetidas para identificar possíveis diferenças nas variáveis PAS e PAD pré-exercício ao longo das 15 sessões de treinamento. Considerou-se o nível de significância de 5%. **Resultados:** Observou-se que, com exceção da quarta e sexta sessões, os níveis de PAS diminuíram em todas as sessões após o exercício ($p \leq 0,05$). Para a PAD, somente houve diminuição significativa após o exercício nas três primeiras sessões. Nos efeitos crônicos, ocorreu redução média nos valores de PAS em repouso ao longo das sessões, com efeito hipotensor acima de 70% a partir da sétima sessão ($p \leq 0,05$). Na PAD, diferenças nos valores em repouso se acentuaram a partir da décima sessão; ao comparar com os valores de PAD em repouso, verificou-se efeito hipotensor acima de 94%. **Conclusão:** Sobreviventes que aderiram ao programa de exercício físico apresentaram redução aguda e crônica da PAS e da PAD.

Palavras-chave: sobreviventes de câncer; pressão arterial; exercício físico.

RESUMEN

Introducción: Pocos estudios han explorado el resultado de los componentes hemodinámicos en sobrevivientes de cáncer en un programa de ejercicio. **Objetivo:** Verificar cambios agudos y crónicos en la presión arterial sistólica (PAS) y diastólica (PAD) durante un programa de ejercicio en sobrevivientes de cáncer de mama. **Método:** En un hospital de referencia, 24 mujeres sobrevivientes participaron en un programa de ejercicio físico. La PA se controló con un monitor de muñeca digital, antes y después de las sesiones. Para las comparaciones antes y después del ejercicio en cada sesión, se utilizó la prueba *t* para muestras pareadas. Para el análisis de efectos crónicos se utilizó el análisis de varianza (Anova), con medidas repetidas para identificar posibles diferencias en las variables de PAS y PAD pre-ejercicio durante las 15 sesiones de entrenamiento. Se consideró un nivel de significancia del 5%. **Resultados:** Se observó que, con excepción de la cuarta y sexta sesión, los niveles de PAS disminuyeron en todas las sesiones después del ejercicio ($p \leq 0,05$). Para DBP, solo hubo una disminución significativa después del ejercicio en las primeras tres sesiones. En los efectos crónicos, hubo una reducción media de los valores de PAS en reposo a lo largo de las sesiones, con un efecto hipotensivo superior al 70% a partir de la séptima sesión ($p \leq 0,05$). En PAD, las diferencias en los valores en reposo aumentaron a partir de la décima sesión; al comparar con los valores de PAD en reposo se observó un efecto hipotensor superior al 94%. **Conclusión:** Los supervivientes que se adherieron al programa de ejercicio físico mostraron una reducción aguda y crónica de la PAS y la PAD.

Palabras clave: sobrevivientes de cáncer; presión arterial; ejercicio físico.

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INTRODUCTION

Recent advances in detecting and treating cancer had positive results as the exponential increase of the number of survivors worldwide¹. However, the main therapeutic resources utilized for the survival (chemotherapy, radiotherapy or both) provoke cardiovascular toxicity requiring multiprofessional attention, mainly in post-treatment follow-up².

According to the literature, cardiotoxicities can be classified per type of oncologic treatment. Within this broad spectrum, chemotherapy agents have been associated with the incidence of hypertension in cancer patients and survivors³. It is also suggested increased risk of vascular dysfunction and consequential hemodynamic unbalance in cancer survivors because the mean vascular age is eight-fold greater than the chronological⁴. Still, the oncologic population or survivors present systemic arterial hypertension (SAH) higher than the general population⁵.

The “*Sociedade Brasileira de Cardiologia*” and “*Sociedade Brasileira de Oncologia Clínica*” has been meeting with specialists to propose evidences-based recommendations and develop multidisciplinary care for proper management of this rising category of patients. In 2019, Brazil hosted the V Global Cardio-Oncology Summit with the participation of 600 professionals (cardiologists, oncologists, hematologists, physical activities professionals, among others)¹.

Cancer and cardiovascular diseases (CVD) share high co-prevalence due to the occurrence of risk factors common to both conditions, among them: smoking, hypertension, obesity, diabetes, unhealthy diet and physical inactivity⁶. The convergence of certain risk factors, in particular, physical inactivity, favors the implementation of integrated intervention strategies whose mechanisms of action are common either for cancer or CVD^{7,8}. There is an expressive body of evidences presenting alterations of acute and chronic blood pressure (BP) with the practice of physical exercises, mainly in older adults and hypertensive^{9,10}. However, intervention studies with breast cancer survivors with the outcome of BP alterations are scarce and have methodological limitations, especially while reporting components of the prescription (frequency, intensity, time and type – FITT) and adherence to the protocol¹¹⁻¹³.

Gaps about the magnitude of the hypotensive effect of exercise in breast cancer survivors exist, considering the possible cardiotoxic effects on the cardiovascular system¹⁴.

The main objective of this study was to investigate acute and chronic alterations of BP during an exercise program in breast cancer survivors.

METHOD

The study participants were enrolled in a visit to a group of psychologic therapy with women cancer survivors who met monthly and who have submitted to breast cancer treatment in a hospital of the city of Maceió (AL), Brazil, classified as High Complexity Oncologic Clinic (Cacon).

At the visit, the proposal of physical exercises in the own hospital area was presented, names and telephone of potential participants were collected for future contact. The proposal consisted in a spinoff of a university extension project called *Com Ação* whose main objective was to investigate the effects of physical exercises intervention on selected health indicators.

Among the breast cancer survivors, 41 were interested and a physical evaluation was scheduled with this group in the hospital assigned area. 32 women responded, of which 24 attended the sessions with mean age of 56.8 years (± 7.7) assigned to three morning sessions.

The Institutional Review Board of the university approved the study, report 3.455.770 (CAAE: 89365218.8.0000.5013). All the participants signed the informed consent form (ICF). The study was reviewed by the hospital's Teaching and Research Division.

PROTOCOL OF INTERVENTION WITH EXERCISES

The program of exercises was applied in-person twice a week and two-days of walking for at least 30 minutes unsupervised. The intensity was monitored through subjective perception of effort (SPE)¹⁵, the scores of moderate intensity (11-13) utilized as reference of ideal load. Each session lasted 40 minutes with aerobics and resistance exercises according to Chart 1.

In this first phase of the program, 24 sessions were distributed in 12 weeks. However, due to COVID-19 pandemic in 2020, the project had to be discontinued in the eighth week and in the fifteenth session. The sessions were conducted by Physical Education students of an university supervised by the project coordinator, a teacher at the institution.

BLOOD PRESSURE MEASURE PROCEDURE

Blood pressure (BP) was measured after the women were seated for 10 minutes and the results logged in a form, they were guided to keep silent during this procedure¹⁶. At the end, the women continued seated and after 10 minutes, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were registered. It was utilized the digital wrist monitor Omron Connect Hem-6232t, with sensor for correct adjustment at the same level of the heart. Though little utilized by clinic routine, it is a valuable tool for the investigation¹⁶.

Chart 1. Description of the structure of the sessions of the exercises program for breast cancer survivors

Component of the session	Duration	Content
Warming	5 min	Dynamic stretching
Main	30 min	
Aerobics	10 min	Aerobic dance or step
Resistance	5 min	At each station, 15 repetitions of the movements with rest and 30-seconds transition: <ul style="list-style-type: none"> • 1st station – squat 90° • 2nd station – shoulder abduction with hand dumbbells • 3rd station – on all fours, with ankle weights, hips extension with flexed knees (alternating) • 4th station – standing, elbow flexion with elastic band • 5th station – upper abdominals holding a stick, flexing the thorax until sticks touches thighs
Repetition of aerobics and resistance	15 min	
Relaxation	5 min	Static stretches lying on the mat, closed eyes, muscles relaxed, listening soft instrumental tunes

Initially, missing data during training sessions were checked for multiple imputation of data through Little's test of missing completely at random (MCAR), fully random. The percentage of missing data for the variables pre-exercise SBP, post-exercise SBP, pre-exercise DBP and post-exercise DBO was 21.0%.

The normality of the data was analyzed through asymmetry and kurtosis values. The data had normal distribution. Descriptive analysis with mean and standard-deviation (SD), absolute and relative frequency were performed. To compare pre and post-exercise in each one of the sessions (acute effects), paired samples t-test was utilized.

ANOVA variance analysis was utilized for chronic effects with repeated measures to identify possible differences in the variables SBP and DBP pre-exercise during 15 training sessions. When the Mauchly's sphericity test was violated, it was assumed the Greenhouse-Geisser correction. Had differences been encountered, the main effects and interaction terms were analyzed using contrasts and Tukey post hoc. The highest value of reference of SBP and DBP in the first week of exercise (first or second training session) was considered for comparison with other training sessions because women were still adapting to training.

The value of SBP at rest of the first training session was considered as reference (132.5±8.6 mmHg) and for DBP, the value of the second training session (82.8±9.4 mmHg). Additionally, the difference between the pressures, the percent variations of pressure differences (D%) and the maximum hypotensive effect (MHE) were calculated, which was stable during the program. The SBP at rest

was compared in the first and last session and the second with the last session of exercise for DBP at rest and it was accepted the difference as 100% of hypotensive effect of the exercise described in percentage, already utilized in the literature¹⁷.

The level of significance of 5% was considered and the Statistical Package for the Social Sciences (SPSS) version 23.0 was adopted for all the analyzes

RESULTS

The sample consisted in 24 women survivors of breast cancer who were 56.8 (±7.7) years old in average and the mean time of diagnosis was 8.1 (±3.8) years. Most of the women investigated was submitted to chemotherapy and radiotherapy (75%) and all of them to surgery. For those with comorbidities (58.3%) the great prevalence was hypertension (64.2%). Overweight and obesity reached 73%. Only 29.2% of the sample dedicated at least 150 minutes of moderate-intensity activity or 75 minutes of strong-intensity activity per week¹⁸, being physically active (Table 1).

There was drop of the SBP at rest (pre-exercise) during the training sessions. The differences in these values became more evident ($p \leq 0.05$) from the seventh session, when comparing with the values of the first session, it was detected a hypotensive effect above 70%. In the following sessions, this drop remained or increased ($p \leq 0.05$) as Table 2 shows.

Reductions of DBP at rest (pre-exercise) were detected during the training sessions. The differences between the DBP values at rest at the fifth and seventh sessions were

lower than in the second session ($p \leq 0.05$). These values increased from the tenth session on when compared to DBP results at rest at the second session, the hypotensive

effect was above 94%. In the following sessions, this decrease continued or decreased even more ($p \leq 0.05$) according to Table 3.

Table 1. Profile of breast cancer survivors submitted to physical exercise program

Characteristics	(n=24)
Age: years, mean (SD)	56.8 (7.7)
Time of diagnosis: years, mean (SD)	8.1 (3.8)
Treatment: n (%)	
Only chemotherapy	3 (12.5%)
Only radiotherapy	3 (12.5%)
Chemotherapy and radiotherapy	18 (75.0%)
Hormone therapy	8 (33.3%)
Surgery	24 (100%)
Comorbidities: n (%)	
Hypertension	9 (37.5%)
Other comorbidities	10 (41.5%)
Without comorbidities	5 (21.0%)
BMI: n (%)	
Normal	6 (24.0%)
Overweight	9 (36.5%)
Obese	9 (36.5%)
Level of physical activity: n (%)	
Physically active	7 (29.2%)
Poorly active	17 (70.8%)

Captions: BMI = Body Mass Index; SD = standard deviation.

With the exception of the fourth and sixth training sessions, the analysis of the acute effects of the training revealed that the levels of SBP declined in all sessions post-exercise ($p \leq 0.05$) as Graph 1A shows. For DBP, there was significant reduction only after exercise in the first three sessions, for the remaining, no pre and post-exercise significant differences were found (Graph 1B).

DISCUSSION

Overall, the post-exercise hypotension (PEH) is detected since the first session^{17,19}. It was found in this study significant drop of SBP in nearly all sessions and of DBS, only in the first three sessions (two weeks), perhaps because diastolic values were already within the normal range.

The sustained effect of pressure reduction (chronic) can occur from two weeks or requiring more prolonged periods¹⁷, a significant dropping was found in SBP at rest from the third week on (fifth session), continuing from the fourth week (seventh session) and for DBP, the dropping was sustained from the fifth week (tenth session).

The same mechanism can explain the role of training in reducing chronic and acute SBP because the frequent increase of the force exerted by the blood in the vascular wall caused by the exercise leads to a continued rise of nitric oxide release and prolonged vasodilation²⁰. It was

Table 2. Comparative results of SBP values at rest (pre-exercise) during the training sessions (reference = 1st session)

Sessions	Mean \pm SD (mmHg)	Difference in mmHg	D%	MHE%	p
2 x 1	130.4 \pm 10.8 x 132.5 \pm 8.6	-2.1	-1.6	23.3	0.41
3 x 1	130.2 \pm 13.1 x 132.5 \pm 8.6	-2.4	-1.7	26.6	0.41
4 x 1	128.7 \pm 16.1 x 132.5 \pm 8.6	-3.8	-3.0	42.2	0.20
5 x 1	126.4 \pm 10.7 x 132.5 \pm 8.6	-6.1	-5.0	67.7	<0.01*
6 x 1	128.4 \pm 12.7 x 132.5 \pm 8.6	-4.1	-3.2	45.5	1.00
7 x 1	126.0 \pm 13.4 x 132.5 \pm 8.6	-6.5	-5.1	72.2	0.03*
8 x 1	125.3 \pm 11.9 x 132.5 \pm 8.6	-7.2	-5.7	80.0	0.01*
9 x 1	126.8 \pm 5.6 x 132.5 \pm 8.6	-5.7	-4.5	63.3	<0.01*
10 x 1	125.9 \pm 12.9 x 132.5 \pm 8.6	-6.5	-5.2	72.2	0.04*
11 x 1	125.7 \pm 13.7 x 132.5 \pm 8.6	-6.8	-5.4	75.5	0.05*
12 x 1	123.2 \pm 14.1 x 132.5 \pm 8.6	-9.3	-7.5	100.0	0.01*
13 x 1	125.4 \pm 14.9 x 132.5 \pm 8.6	-7.1	-5.7	78.8	0.05*
14 x 1	124.1 \pm 9.2 x 132.5 \pm 8.6	-8.4	-6.8	99.5	<0.01*
15 x 1	123.5 \pm 11.0 x 132.5 \pm 8.6	-9.0	-7.2	100.0	<0.01*

Captions: SD = standard-deviation; D% = variation of BP in percentage; MHE% = expressed maximum hypotensive effect in percentage.

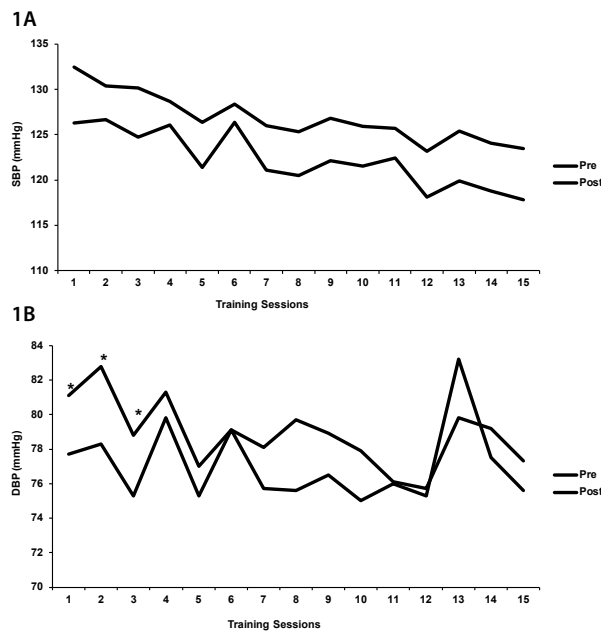
(*) $p \leq 0.05$: repeated-measures analysis of variance – post hoc Tukey.

Table 3. Comparative results of DBP values at rest (pre-exercise) during the training sessions (reference = 2nd session)

Sessions	Mean ± SD (mmHg)	Difference (mmHg)	D%	MHE%	p
1 x 2	81.1±4.5 x 82.8±9.4	-1.7	-2.0	98.0	0.41
3 x 2	78.9±10.5 x 82.8±9.4	-3.9	-5.0	95.2	0.07
4 x 2	81.3±13.6 x 82.8±9.4	-1.5	-1.8	98.1	0.57
5 x 2	77.0±6.7 x 82.8±9.4	-5.8	-7.5	93.0	0.02*
6 x 2	79.1±11.4 x 82.8±9.4	-3.6	-4.7	95.5	0.14
7 x 2	78.1±8.4 x 82.8±9.4	-4.7	-6.0	94.3	0.03*
8 x 2	79.7±10.8 x 82.8±9.4	-3.1	-4.0	96.2	0.08
9 x 2	79.0±4.1 x 82.8±9.4	-3.8	-4.8	95.4	0.07
10 x 2	78.0±9.0 x 82.8±9.4	-4.8	-6.2	94.3	<0.01*
11 x 2	76.1±8.6 x 82.8±9.4	-6.7	-8.8	92.0	<0.01*
12 x 2	75.7±8.7 x 82.8±9.4	-7.1	-9.3	91.4	<0.01*
13 x 2	79.8±10.5 x 82.8±9.4	-2.9	-3.7	96.3	0.16
14 x 2	79.2±5.8 x 82.8±9.4	-3.6	-4.5	95.6	0.04*
15 x 2	77.3±9.5 x 82.8±9.4	-5.5	-7.1	100.0	<0.01*

Captions: SD = standard-deviation; D% = variation of BP in percentage; MHE% = expressed maximum hypotensive effect in percentage.

(*) p≤0.05: repeated-measures analysis of variance – post hoc Tukey.



Graph 1. Comparison of values of SBP (1A) and DBP (1B) pre and post exercise

(*) p≤0.05: test t for paired samples.

also detected that training causes systemic adaptation of the arterial wall that can translate in better arterial compliance, facilitating the reduction of the peripheral resistance after a single session of exercise²¹.

Considering that individuals after the diagnosis of cancer have particularly high rate of hypertension²², that the estimate of survivors classified as physically active ranging between 20%-30% in Canada, 30% in

the USA, 22% in Germany and 15% in Australia²³ and that evidences are still insufficient in this subgroup²⁴, intervention strategies should facilitate the adherence to exercise programs.

The proposals for physical exercise programs should be based in the literature addressing association of components FITT with outcomes in health indicators both in oncologic and hypertensive patients^{8,10,25}.

Findings of the literature are dissimilar about the magnitude and duration of post-exercise hypotension (PEH) – despite this effect can persist for until 48 hours, the magnitude of its reduction is bigger in the first hours after the exercise²¹. Thus, the program was designed with a frequency of four-days a week, twice in-person supervised in a hospital room where the oncologic treatment was conducted and twice as unsupervised walking in an area preferred by the survivor and recorded by the coordinating team. Having fatigue as clinical outcome, a breast cancer survivor centered physical exercise program twice a week and modified to remote due to the COVID-19 pandemic did not reduce significantly the fatigue²⁶.

The intensity is essential for dose control (physical stimuli), nevertheless, there are evidences that for PEH, what matters is the volume and not the intensity of the exercise²⁰. A recent meta-analysis which investigated the acute effects of aerobic and resistance training in hypertensive and normotensive patients found PEH independent of the intensity and for aerobics, the load applied was between 40%-75% of the maximum heart rate and for resistance, between 40%-80% of one maximum repetition (1RM)²⁷.

Typically, the intensity recommended for outcomes on BP for aerobics is from 40% to <60% of the VO_2 maximum, corresponding to approximately 11-14 of the Borg Rating of Perceived Exertion (RPE) considered moderate²⁸ – this cutoff was utilized in the referenced protocol for aerobics control. Aerobic dance and step were chosen as aerobics, the beats per minute (bpm) is an important tool to keep intensity moderate, with choreography and tunes with nearly 130-140 bpm²⁹.

Evidences indicate that regarding the intensity of resistance exercises, loads close to 50% of 1RM promote better autonomic cardiac response than loads of 70% or more of 1RM^{17,30}. Lower loads facilitate the execution of the movement faster and can provide more bioavailability of vasodilator substance as nitric oxide in older women³¹. The protocol determined 15 repetitions for each resistance exercise (30 seconds at each station), approximately 60% of 1RM, with 45-seconds interval from one to the next station. Adjustments to the load were made after monitoring according to the subjective measure of effort, where the score 11-14 (moderate) is the ideal²⁸.

The duration of exercise programs with hypotensive effects reported in the literature is 30-60 minutes per session¹⁰. A 45-minutes session caused bigger BP drop and more lasting when compared to 25-minutes sessions as well as with accumulated time of exercises of until 210 minutes weekly^{32,33}. The intervention was designed as 40-minutes sessions, reaching 160 minutes per week.

Aerobic exercises in first place reduce blood pressure more and resistance exercises come in second¹⁷. In the last years, the investigation about concurrent training in hemodynamic outcomes (combination of aerobic and resistance training in the same session) has been increasing with results close or similar to aerobics and greater than resistance²⁷.

In a meta-analysis investigating the hypotensive effect of concurrent training, bigger reductions of SBP and DBP were found in hypertensive (5/6 mmHg), followed by pre-hypertensive (3/4 mmHg) and unchanged in normotensive samples³⁴. Considering that a physical exercise program for cancer survivors addresses prevention of oncologic-treatment related cardiotoxicity, not only those with high BP will benefit¹.

Concurring training can be prescribed according to different strategies and there is no consensus in the literature despite recent findings of a meta-analysis about the effects in post-exercise hypotension (PEH) regardless of the protocol described²⁷. The aerobic component was present first in the protocol as rhythmic movements (dance, aerobic dance or step) and then resistance exercises as circuit training, which produced better results for arterial compliance³⁵.

Important clinical implications were raised in this study. With the increase of survivorship, recent evidences have already addressed the outcomes of physical exercise as anxiety, fatigue, lymphedema, sleep disorders²³ and particularly the effects on blood pressure levels, broadening the therapeutic scope of cardio-oncology^{22,36}.

With the objective of expanding the offer of therapeutic actions, mainly in the implementation of physical exercises program, public universities attempted to work concurrently with health services.

The study baseline sample failed to enroll only sedentary individuals and without control group, which is one of its limitations, in addition to enrolling hypertensive and normotensive survivors for the intervention; however, due to the cardiotoxicity of the oncologic treatment, the exercise is a primary and secondary prevention, and the longitudinal monitoring of blood pressure is one of the tools proving the protective effect. For future interventions, the sample needs to be expanded which can lead to stronger adherence as the project is intended to be continuous, further to the offer of services to patients in treatment and other types of cancer.

Based in a recent systematic review, the interventions with physical exercises and cancer present strong evidence bases to support their inclusion across all the stages of the cancer treatment plan in a large variety of clinical outcomes, regardless of the type, being necessary efforts to strengthen the protocols of exercises, observing the nuances of the prescription and integration in oncologic care services³⁷.

CONCLUSION

This study demonstrated the positive impact the physical exercise had in the acute and chronic clinical outcome of SBP and DBP in breast cancer survivors. As the sample consisted in hypertensive and normotensive survivors, it is possible to suggest that this type of intervention contributes to the overall vascular health and hemodynamic, minimizing possible extensive oncologic treatment adverse events.

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CONTRIBUTIONS

All the authors contributed substantially to the study design and conception, analysis and interpretation of the

data, wording and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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