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Original Article

Effects of chemotherapy treatment on muscle strength indicators, functional capacity and biopsychosocial aspects of women with breast cancer

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Abstract: Evidences on the effects of chemotherapy treatment cycles on measures of muscle, mental state, social and cognitive performance are scarce. The objective of this study was to analyze the effects of chemotherapy cycles on muscle strength and activation, functional capacity, quality of life, fatigue and anxiety of women with breast cancer. Therefore, twenty-two women divided into a treatment group (n = 10; 46.6 ± 9.6 years) and control group (n = 12; 51.6 ± 7.0 years) participated in the study. Analysis of muscle performance, quality of life, fatigue and anxiety after the 2nd and 4th cycle of chemotherapy with anthracyclines were performed in women with breast cancer (TRA) and compared to healthy women (CTR). Two-way ANOVA was used to compare the variance of the means and the significance level was set as P≤0.05. The results showed Differences in the muscular activation of the *vastus medialis* between the groups at post time (P = 0.038), as well as in the sit and stand test in the baseline (P<0.001) and post moment (P<0.001). Functional capacity performance was different between baseline (P<0.001) and post-time (P<0.001) groups. Additionally, the TRA group worsened the quality of life in the domains of functional capacity (P<0.001) and limitation of physical aspects (P = 0.002), besides presenting negative changes in fatigue. Thus, anthracycline chemotherapy cycles reduce muscular performance and affect biopsychosocial variables in women with breast cancer.

Keywords: Chemotherapy, anthracyclines, muscle strength, quality of life

Introduction

Among the different types, breast cancer has a higher prevalence in women, with risk factors associated with chronic such as endocrine and reproductive diseases [1]. Breast cancer is as well as associated with lifestyle, previous pregnancy, familiar history, ethnicity, prolonged exposure to endogenous estrogens, obesity, as well as sedentary lifestyle and smoking [2]. Currently, the main forms of treatment involve surgery for tumor removal, (neoadjuvant or adjuvant) chemotherapy, radiotherapy, hormone therapy and immunobiological agents, with chemotherapy being the most advanced and safe [3].

Chemotherapy treatment has been shown to demonstrated efficiency in combating the disease, this treatment consists of cycles in which are used different combinations of medications, such as anthracyclines and taxanes over an average period of 24 weeks [4]. However, due to the toxicity of chemotherapy treatment at the cellular level, patients have side effects such as alopecia, anemia, vomiting, premature menopause, weight gain and increased fatigue, which can negatively impact the continuity of treatment [5].

In addition, some studies have shown changes in parameters related to muscle strength (MS) production resulting from the use of taxanes, as peripheral neuropathy [6], influencing overall physical fitness [7], reducing functional capacity (FC) and promoting negative changes on body composition [8, 9]. Klassen et al. [10] analyzed the effects of chemotherapy treatment on mus-

Table 1. Characterization of volunteers (n = 22)

Groups*	Age (years)	Height (cm)	Body mass (kg)	BMI (kg/m^2)	Treatment
TRT	46.6 ± 9.6	1.54 ± 0.6	59.4 ± 5.9	24.9 ± 2.5	AC
CTR	51.6 ± 7.0	1.56 ± 0.3	63.3 ± 9.7	25.9 ± 3.7	N/T

TRT = Treatment group; CTR = Control group; BMI = Body mass index; AC = Anthracycline clycles; N/T = No treatment. *t-Test showed (no) differences between groups at baseline for these variables (P<0.05).

cle strength measurements in women with breast cancer using an isokinetic dynamometer, and identified a loss of up to 25% in strength responses and joint disfunction after treatment. However, due its cross-sectional design, the study did not present sufficient evidence to predict from which course of treatment the reductions in MS occur.

Chemotherapy treatment affect biopsychosocial parameters, which can be defined as subjective variables inherent to the individual's behavior in relation to external factors, by which they can alter their temporary and chronic state in the biological, psychological and social spheres [11-13]. This therapy changes levels of fatigue, anxiety and quality of life [14-20], compromising the prognosis of individuals with cancer.

Despite evidence on adverse effects of chemotherapy [21], to date is unclear when this treatment begins to affect muscle strength, functional capacity and biopsychosocial responses. Therefore, the aim of the present study was to analyze the effects of anthracycline chemotherapy cycles on MS and activation, FC, subjective perception of exertion, quality of life variables, fatigue, and anxiety.

Materials and methods

Participants

The characteristics of the volunteers are described in **Table 1**. The sample size calculation was performed using G***power* version 3.1.9. 4th software [22]. Considering an effect size of 0.6 (ES) with a power of 0.8 and significance of 0.05, a total of 20 participants (10 in each group) would be required. Therefore, 22 women were recruited, considering 10% more for possible loss. Volunteers were separated into treatment group (TRA) and control group (CTR) as described by (n = 10 and 12, respectively) (**Table 1**).

The inclusion criteria of the volunteers for the TRA group were: to be between 30 and 70 years old; to be diagnosed with breast cancer; be between the 2nd and 3rd cycle of chemotherapy; to have medical release for physical exercise; not practicing any type of physical exercise. For the CTR group, the volunteers should: be between 30 and 70 years old; have medical clearance to perform physical exercise; not practice any kind of physical exercise and had no breast cancer diagnosis. Exclusion criteria were: hypertension; uncontrolled cardiovascular diseases; diabetes; metastasis; previous diagnosis of another type of cancer and/or orthopedic limitations that could compromise the execution of the study protocol (**Figure 1**).

The present study was approved by the Research Ethics Committee of the Federal University of Goiás (CAAE: 50717115.4.0000.5083), and by the Research Ethics Committee of the Hospital of Clinicals (HC/UFG) (CAAE: 50717115.4.3001.5078) accordance with the requirement of resolution 466/12 of the National Health Council.

Experimental design

A design research was carried out adapted from an Open-label trial with no-treatment external concurrent control.

The women from TRT were assisted by physician during chemotherapy cycles, the administration of the drugs was performed every 21 days, composed of the drugs doxorubicin and epirubicin, belonging to the group of anthracycline. The evaluations were performed between 20 and 21 days to minimize the acute effects of chemotherapy. The women in the CTR group performed only the evaluations and did not practice any type of physical exercise during the research period.

The volunteers from both groups (TRT and CTR) were submitted to the same tests. For the TRA

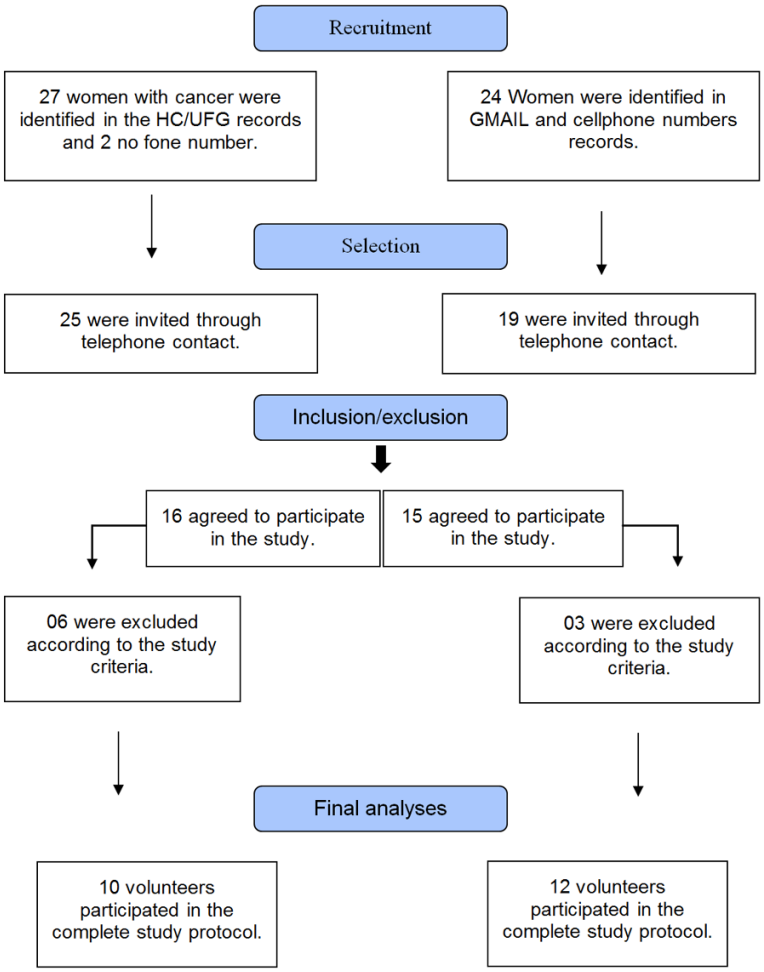

Figure 1. The flow chart of participants enrolled in the study. HC = Hospital of clinics; FUG = Federal University of Goiás; HMAL = human movement assessment laboratory.

group, the measurements occurred between the 2nd and 3rd chemotherapy cycle (QT1) and after the 4th cycle (QT4) (**Figure 2**).

For the CTR group, the same time interval adopted in the TRT group was used. All the visits during the evaluations period were previously and individually scheduled. At the first visit, all the volunteers signed the free and informed consent form, filled an anamnesis, and were exposed to: i) anthropometric measurements, ii) evaluation of muscle activation through electromyography, iii) functional capacity tests, and finally, they answered the quality of life questionnaires (SF-360029 [23], Piper fatigue scale [24], state-trait-state anxiety inventory (STAI) [25], and this moment was called baseline. In the second visit, approximately 42 days after the baseline, the same measurements were performed.

Anthropometric measurements

Body mass was evaluated using an electronic/digital scale with accuracy of 50 grams (minimum weight 1.05 kg and maximum 150 kg; Brand Lider®, model P-150M, (Araçatuba, Brazil). Height was measured by means of a professional stadiometer, with measurement field from 40 to 210 cm (Professional Sanny model ES2030; São Bernado do Campo, Brazil). With these two variables, the body mass index (BMI) was calculated, using the following equation: BMI = Body mass (kg)/Height (m^2) [26].

Evaluation of muscle performance

Muscle activation and subjective perception of exertion

Miotec Medical Equipment Ltda was used to evaluate muscle® activation. All electrode fixation procedures followed the recommendations of the International Society of Electrophysiology and Kinesiology (SIEC) and superficial electromyography for noninvasive muscle evaluation (SENIAM) [27]. The tetrapolar surface electrodes were placed in the rectus femoris (RF) and vastus medialis (VM) muscles according to SENIAM recommendations [27]. Additionally, the activation average adjusted by the activation peak in microvolts (μV) was reported.

Data were collected during the sit and stand test, a randomization was performed to choose the lower limb to fix the electrodes, in order to avoid differences in performance between dominant and non-dominant lower limbs.

The 6-20 Borg scale was used to assess the subjective perception of exertion [28], subdivided into perceptions of effort, as follows: 6 to 8 very, very light, 9 to 10 very light, 11 to 12 fairly light, 13 to 14 somewhat hard, 15 to 16

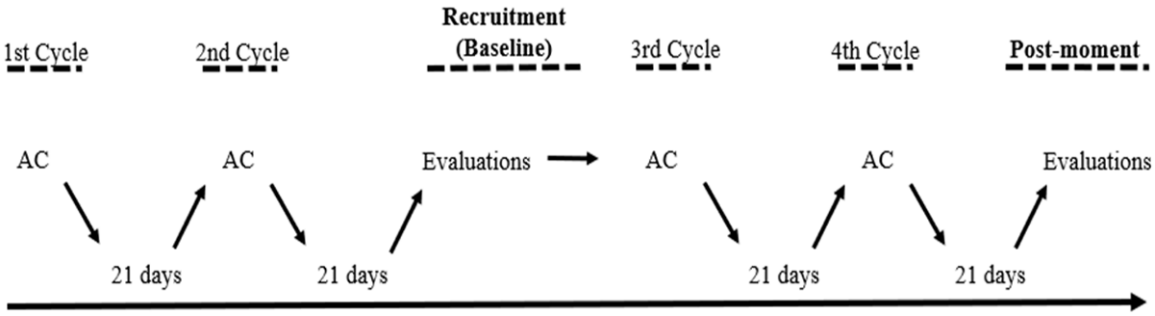

Figure 2. Experimental design of the study.

hard, 17 to 18 very hard and 19 to 20 very, very hard [29]. The volunteers were asked about the perception of effort resulting from the performance of the sit and stand test.

Functional capacity and muscle strength

The muscle strength and functional capacity were performed in faculty of nutrition and health at the Federal University of Goiás. The evaluations were carried out in a room with non-slip floor, always in the morning with the same evaluator at all times. A training was previously performed by the evaluator in order to avoid vies. Were conducted these X tests:

1) Sit and stand test: In test were used, as well as the timed up and go (TUG) according to the protocol proposed by Rikli and Jones [30]. In the test of sit and stand the volunteers should sit and get up from a chair, thus completing 1 repetition.

The volunteers were verbally encouraged to complete the highest number of repetitions (score) during 30 seconds.

2) Time up and go (TUG): at the sign of the evaluator, the volunteers got up from the chair, walked straight for 3 meters and returned to the initial position. The performance was evaluated taking into account the time (seconds) used to perform the task [21, 30].

Evaluation of biopsychosocial parameters

The SF-36 instrument was used (Medical Outcomes Study 36 - Item Short-Form Health Survey) version in Portuguese [31] was used to assess the quality of life. This instrument presents 36 items divided into 8 domains: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality, social functioning (SF), role emotional aspects (RE), mental health (MH), classified on a scale from 0 to 100. Additionally, the SF-36 has reliability and validity for populations with cancer [32].

Fatigue was assessed using the Fatigue Scale questionnaire of Piper et al. [24] composed of 22 items subdivided into four different subjective dimensions: affective, sensory, cognitive and behavioral. Scores can range from 0 (zero) to 10 (ten), where: 0 - represents absence of fatigue; 1 to 3 - average level of fatigue; 4 to 6 - moderate levels of fatigue; 7 to 10 - severe fatigue levels. Additionally, the fatigue scale questionnaire has reliability and validity for populations with cancer [24].

The trait-State Anxiety inventory used to assess anxiety is composed of two distinct self-report scales to measure two distinct concepts of anxiety: state of anxiety (A-state) consisting of the individual's daily perception and anxiety trait (A-trait) referring to the individual's perception at that very moment. Both are composed of 20 questions. Additionally, the trait-state anxiety inventory has reliability and validity for populations with cancer [33].

Statistical analysis

Parametric data are presented in mean ± standard deviation (SD), while nonparametric data are presented in median ± standard error. Data normality was tested using Shapiro-wilk test. The t-independent test was used to compare the characterization variables between groups at baseline. The two-way ANOVA (2×2) was used to compare the variance of the means between the moments. When necessary, the Bonferroni *post-hoc* test was used to find the differences.

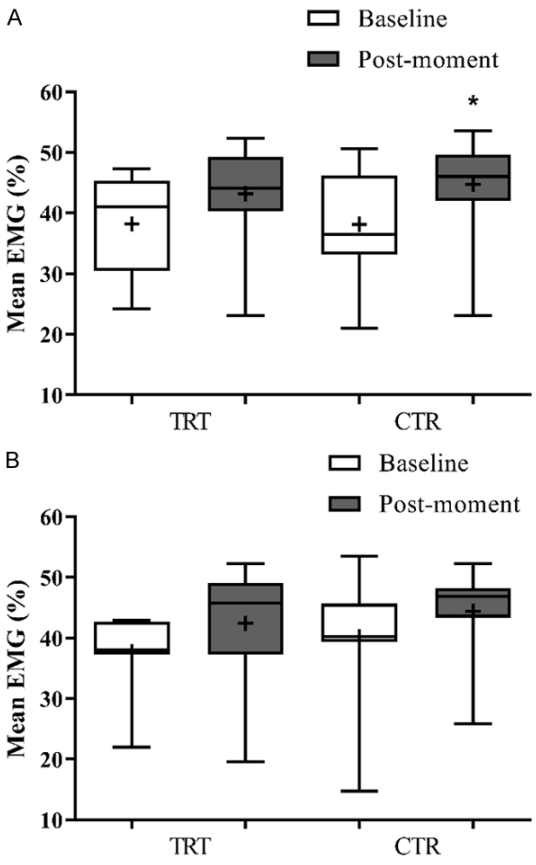

Figure 3. Comparison of the mean EMG (%). A. Vastus medialis; B. Rectus femoris. TRT = treatment group; CTR = control group; Values are presented as median (lines) with interquartile range (boxes) ± range (minimum and maximum) and + indicates mean *P<0.05 compared to TRT.

Additionally, the Cohen's *d* effect of size [36] was calculated from the difference between groups to examine the magnitude of breast cancer treatment. The *d* values obtained were used to define the effect size as trivial (d<0.2), small (0.2<d<0.5), medium (0.5<d<0.8) and large (d>0.8) [34].

All analyses were performed using the *Statistical Package for the Social Sciences* (SPSS) version 20.0. The significance level of P≤0.05 was used.

Results and discussion

Two-way ANOVA demonstrated that muscle activation of VM in the TRT group was significantly lower compared to the CTR group at the time after (36.4 ± 2.8 μV e 46.0 ± 1.7 μV; P = 0.038; d = 0.27). However, no significant differences were found in the electromyographic activity of RF in any moment (**Figure 3**).

Additionally, although no differences were found in the electromyographic activity of the RF, the TRT group showed lower percentage values (%) activation at all times compared to CTR (**Table 2**).

No significant differences were found in the subjective perception of exertion during sit and stand test between the TRT and CTR groups at baseline (10.0 ± 2.6 au and 11.8 ± 3.1 au, respectively) and post (11.0 ± 2.8 au and 11.7 ± 3.1 au, respectively), as well as between intragroup values.

However, compared to the TRT group, the CTR group performed better in the sit and stand test at baseline (17.6 ± 3.7 reps e 29.1 ± 4.2 reps, respectively, P<0.001; d = -0.42) and post-moment (18.5 ± 2.6 reps e 28.5 ± 2.4 reps, respectively, P<0.001; d = -0.42). However, no intragroup difference (**Figure 4**).

In addition, compared to the TRT group, the CTR group performed better in the TUG test at baseline (6.1 ± 0.6 sec and 5.3 ± 0.3 sec, respectively; P<0.001; d = 0.11) and post moment (TRT = 6.0 ± 0.4 sec and CRT = 4.9 ± 0.5; P<0.001; d = 0.11), however, no intragroup differences were found (**Figure 5**).

The TRT group reduced the quality of life scores, specifically PF domain between *baseline* and post-moment [F(1;40) = 8.33; d = 1.41; P = 0.006], as well as increased scores in the domain of RP [F(1;40) = 33.94; d = -0.73; P<0.001]. However, no significant changes were found in the other domains between moments and/or groups (**Table 3**).

From this perspective, the results related to fatigue show that a percentage part of the TRT group had moderate levels of fatigue in all domains in the baseline and post-moment, while only a small percentage of the CTR group showed similar levels only in the sensory and cognitive domains. Additionally, some volunteers from the TRT group presented severe levels of fatigue in the behavioral and affective domains (**Table 4**). However, the results related to A-trait and A-state anxiety were similar between groups and moments (**Table 4**).

Table 2. Comparison EMG peak mean (μV)

Group	Moment			
	TRT		CTR	
	Baseline	Post-moment	Baseline	Post-moment
RF	37.7 ± 6.1	40.2 ± 10.2	42.4 ± 10.3	44.4 ± 7.8
VM	38.2 ± 8.7	36.2 ± 13.7	42.4 ± 8.2	44.8 ± 7.8

TRT = treatment group; CTR = control group; RF = rectus femoris; VM = vastus medialis.

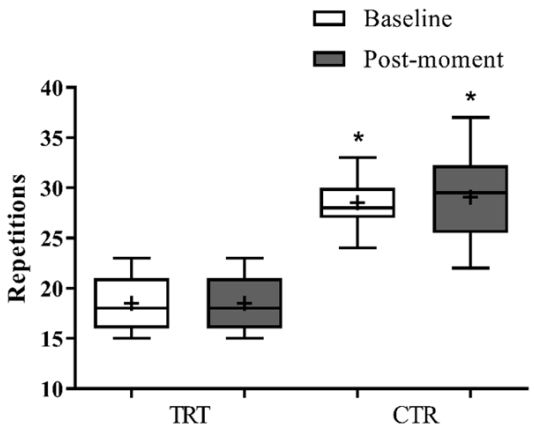

Figure 4. Comparison of the sit and stand test. TRT = treatment group; CRT = control group; Values are presented as median (lines) with interquartile range (boxes) ± range (minimum and maximum) and + indicates mean *P<0.05 compared to TRT.

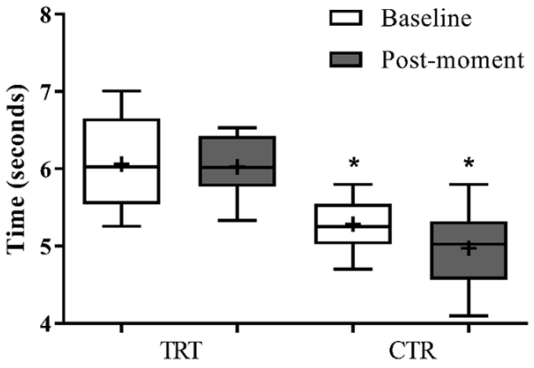

Figure 5. Comparison of the test timed up and go. TRA = treatment group; CTR = control group; Values are presented as median (lines) with interquartile range (boxes) ± range (minimum and maximum) and + indicates mean *P<0.05 compared to TRT.

Discussion

The aim of this study was to analyze and compare the effects of chemotherapy cycles with anthracyclines on activation and MS, FC, effort perception, quality of life, fatigue and anxiety indicators. The results show significant differences between the groups in the muscle activation of VM, as well as in the MS evaluated by the sit and lift test and FC by the TUG test. In addition, the TRT group worsened some domains of quality of life, well as showed an increase in fatigue rates.

Despite the existence of some evidence on the possible side effects of chemotherapy treatment in MS parameters [10]. Our results are unprecedented in demonstrating changes in muscle activation, MS, FC and biopsychosocial parameters between chemotherapy cycles with anthracyclines.

However, Klassen et al. [10] compared the strength levels of 255 women at different stages of chemotherapy treatment, the researchers demonstrated that women initiating chemotherapy had higher levels of MS compared to women after treatment, although no evaluations were performed between chemotherapy cycles, these findings corroborate our study by demonstrating that at some point in chemotherapy treatment there was a reduction in MS.

Interestingly, results contrary to ours were found by Marques [35], when performing a comparison with women who were between the 2nd and 3rd cycle of chemotherapy with women considered healthy in MS measurements using the isokinetic device, the results did not show differences in torque measurements, as well as total work between groups. Possibly, the protocol used in isokinetics, in addition to the little functionality of the motor gesture (knee extension), may have contributed to these results.

In this sense, the differences in muscle performance found in our study in the sit and raise tests (MMII strength) and in the TUG test (FC) between the 2nd and 3rd, as well as after the 4th cycle, can be justified by the similarity of the tests with the day-to-day activities, a factor that can contribute to a better analysis of muscle performance linked to the aspect of CF when compared to isokinetic.

Additionally, the results found in the sit and raise test in the TRT group of the baseline (18,1 ± 3,5) and post moment (18,5 ± 2,6), surprisingly, are similar to the normative values of the elderly (10-22,6 repetitions) age group between 60-69 years [36], extoling the temperature of anthracycline cycles, taking into account that

Table 3. Comparison quality of life inter and intra groups

Variable	Group TRT (n = 10)				Group CRT (n = 12)				p*
	Baseline	Pós	P#	Effect size	Baseline	Pós	p#	Effect size	Group x Moment
	Mean ± DP	Mean ± DP			Mean ± DP	Mean ± DP			
Quality of life									
Physical functioning	77.0 ± 16.9§	58.7 ± 11.6§	0.01#	-1.26	88.1 ± 7.2	85.9 ± 10.2	0.65	-0.25	0.03*
Role physical	12.5 ± 13.2	45.7 ± 45.5	0.02#	0.99	81.4 ± 26.3	81.7 ± 26.3	0.98	0.01	0.07
Bodily pain	63.0 ± 33.7	57.9 ± 17.3	0.64	-0.19	71.6 ± 24.7	73.5 ± 17.6	0.85	0.09	0.64
General health	59.8 ± 18.9	67.0 ± 20.1	0.31	0.37	72.0 ± 11.6	74.8 ± 12.1	0.66	0.24	0.65
Vitality	53.5 ± 17.1	64.0 ± 24.9	0.06	0.49	68.1 ± 13.0	69.0 ± 11.4	0.49	0.07	0.35
Social functioning	75.1 ± 22.8	68.3 ± 38.4	0.55	-0.22	81.7 ± 21.6	85.6 ± 14.6	0.70	0.21	0.49
Role emotional	40.0 ± 41.0	44.6 ± 41.6	0.78	0.11	76.1 ± 35.1	74.3 ± 31.2	0.90	-0.05	0.77
Mental health	66.8 ± 22.6	65.4 ± 23.3	0.86	-0.06	73.0 ± 12.5	69.1 ± 13.0	0.62	-0.31	0.83
General status	56.0 ± 16.3	59.2 ± 21.9	0.62	0.17	76.6 ± 9.9	76.7 ± 7.5	0.97	0.01	0.73

TRT = treatment group; CTR = control group; § = P<0.05 compared to the same moment in the CRT; # = P<0.05 compared to baseline; * = interaction between group and moment.

the TRT group was of lower age (46,6 ± 9,6), with less exposure to the inherent factors of aging, which contribute to compromise muscle performance.

In addition, the lower results of the TRT group in the TUG test may suggest increased cardiovascular risk, Saraiva et al. [37] found that better tug test performances, such as a decrease of 0.7 seconds in the performance of the test is associated with the increase in relative manual pressure strength, and this parameter is an important marker of mortality due to cardiovascular disease [38].

Although our study did not evaluate the relative handgrip strength, however, considering that anthracyclines are also associated with the incidence of cardiovascular diseases [39], the difference found between the TRT and CRT groups in the TUG test probably demonstrates an indication of increased cardiovascular risk, and therefore, these findings could contribute to the use of the TUG test for this purpose or similar during chemotherapy.

Furthermore, the results of muscle activation, which is also related to muscle performance, showed a reduction in the muscle activation of the vastus medial in the TRT group after the 4th cycle, demonstrating that chemotherapy treatment with anthracyclines may compromise the neuromuscular function of the knee extensor muscles.

Although no research has been found with analyses of muscle activation during chemotherapy treatment similar to ours, but only in other phases of treatment, such as surgical [40, 41].

Our findings are important in the perspective of relating the reduction of muscle activation due to treatment, with low FC and/or MS Pion et al. [42] demonstrated that morphological markers such as phenotype (type and proportion of fibers), architecture (muscle thickness and angle of pity) and/or muscle mechanisms (contraction and relaxation time), do not explain the reduction of FC, but neuromuscular parameters such as muscle activation, corroborating our study regarding VM activation.

However, no differences were found in the muscle activation of the rectus femoris, possibly the specificity of the sitting and lifting test may have compromised the results, since in this movement, the rectus femoris shows less request when compared to quadriceps muscles [43]. However, corroborating the researches mentioned above, our VM results support that the analysis of quadriceps muscle activation may be an important assessment to be used during chemotherapy treatment in order to monitor neuromuscular factors sensitive to changes in FC.

Among these factors, it is possible that muscle activation may be altered by chemotherapy due

Table 4. Distribution (%) of fatigue and anxiety domains baseline and post-moment

Domain	Fatigue level	Groups			
		TRT		CRT	
		Baseline	Post-moment	Baseline	Post-moment
Behavioral	Absence	------	------	------	------
	Middle	60.0% (n = 6)	50.0% (n = 5)	100.0% (n = 12)	100.0% (n = 12)
	Moderate	40.0% (n = 4)	20.0% (n = 2)	------	------
	Severe	------	30.0% (n = 3)	------	------
Affective	Absence	------	------	------	------
	Middle	60.0% (n = 6)	50.0% (n = 5)	100.0% (n = 12)	100.0% (n = 12)
	Moderate	20.0% (n = 2)	40.0% (n = 4)	------	------
	Severe	20.0% (n = 2)	10.0% (n = 1)	------	------
Sensory	Absence	------	------	------	------
	Middle	70.0% (n = 7)	70.0% (n = 7)	100.0% (n = 12)	83.3% (n = 7)
	Moderate	30.0% (n = 7)	30.0% (n = 7)	------	16.7% (n = 2)
	Severe	------	------	------	------
Cognitive	Absence	------	------	------	------
	Middle	80.0% (n = 8)	80.0% (n = 8)	91.7% (n = 11)	100.0% (n = 12)
	Moderate	20.0% (n = 2)	20.0% (n = 2)	8.3% (n = 1)	------
	Severe	------	------	------	------
General mean	Absence	------	------	------	------
	Middle	60.0% (n = 6)	50.0% (n = 5)	100.0% (n = 12)	100.0% (n = 12)
	Moderate	40.0% (n = 4)	50.0% (n = 5)	------	------
	Severe	------	------	------	------
Domain	Anxiety level				
Trace	Low	40.0% (n = 4)	30.0% (n = 3)	41.7% (n = 5)	33.3% (n = 4)
	Moderate	60.0% (n = 6)	50.0% (n = 5)	58.3% (n = 7)	58.3% (n = 7)
	High	------	20.0% (n = 2)	------	8.3% (n = 1)
	Severe	------	------	------	------
State	Low	40.0% (n = 4)	20.0% (n = 2)	33.3% (n = 4)	41.7% (n = 5)
	Moderate	50.0% (n = 5)	70.0% (n = 7)	66.7% (n = 8)	50.0% (n = 6)
	High	10.0% (n = 1)	10.0% (n = 1)	------	8.3% (n = 1)
	Severe	------	------	------	------

*The data is shown as relative frequency (absolute frequency).

to its action on skeletal muscle such as molecular alterations, including the ubiquitin-proteasome pathway, autophagy, IGF-1/PI3K/Akt/mTOR, IL-6/JAK/STAT and NF-κB [44]. In addition to these factors, a decrease in the cross-sectional area of the vastus inherent to the reduction of type II fibers in patients with breast cancer has been previously reported [45]. Therefore, these alterations may partly explain the decrease in vastus muscle activation found in our study.

Furthermore, the assessment of the subjective perception of exertion performed concomitantly with the sit-and-raise test, as well as EMG, did not show significant differences (classification of "relatively easy" at all times) despite the research conducted by Fernandez et al. [46] correlate the subjective perception of exertion with central fatigue in patients diagnosed with cancer, our results suggest that chemotherapy cycles with anthracyclines do not alter these parameters.

However, other manifestations of fatigue seem to worsen due to treatment, our findings showed that 30% of women after the 4th cycle of chemotherapy with anthracycline presented severe levels of fatigue in the behavioral domain and 10% in the affective domain (**Table**

4). These results corroborate Jacobsen et al. [47] who found that in addition to the individuals with fatigue at the beginning of treatment, they presented worsening of their condition at the end of chemotherapy.

Additionally, the percentage of women in the general mean domain of the TRT group with moderate levels of fatigue at baseline (40%), just as at the time post (50%), may be justified by several aggravating factors of cancer-related fatigue, such as increased concentration of pro-inflammatory cytosines, sleep disorders and increased cortisol [48, 49].

Therefore, our findings are important in showing that fatigue problems are found after the 2nd cycle of chemotherapy, these findings may offer support for the implementation of resources aimed at controlling or reversing fatigue rates and other parameters such as anxiety.

Ferreira et al. [50] analyzing 233 patients using an instrument different from ours to assess anxiety during treatment in different types of cancer, a prevalence of anxiety of 26.18% was found, although our study did not present "severe" levels of anxiety, between 50% and 70% of individuals in the TRT group demonstrated "moderate" levels of anxiety of the trait or state type, similar results were found in the CRT group (**Table 4**). However, we emphasize that our findings correspond only to the period of cycles with anthracyclines, since there is evidence suggesting problems in anxiety levels during complete treatment with association with physical inactivity, anxiolytic medication, breast swelling and/or advanced stage of the disease [51].

Despite this, Villar et al. [51] demonstrated that anxiety levels decrease soon after the end of treatment, however, this study performed evaluations before the cycles and at the end of the complete treatment, as our results did not highlight differences between the groups, possibly anxiety is evident after anthracycline cycles with possible decrease at the end of treatment.

In addition, Silva, Zandonade e Amorim [52], interestingly, they found that individuals presenting "moderate" levels of anxiety similar to those of our study at the beginning of chemotherapy, develop a strategy to cope with the disease, which can negatively interfere in other variables such as quality of life, therefore, in the efficiency of treatment.

The TRT group of our study showed significant reductions in the FC Domain of quality of life, in addition, the CRT group showed better baseline and post-moment scores. Although there are few studies evaluating quality of life during chemotherapy cycles in individuals with breast cancer, recent evidence presented by Klapheke et al. [53] comparing 3 different types of cancer (cervical, ovary and uterus) demonstrated a decrease in quality of life domains similar to FC regardless of type of cancer, treatment or time of diagnosis.

However, this relationship seems to be influenced by some factors, recently Hassen et al. [54] conducted a research in Ethiopia in order to associate several domains of quality of life with chemotherapy cycles and sociodemographic factors, curiously the domains less affected by chemotherapy cycles were those linked to physical characteristics/FC, while the most affected were linked to emotional aspects, corroborating other studies [55, 56].

In this sense, the results contrary to those found in our study can be explained by the sociodemographic factors of the countries to which the research were conducted, for example, in Ethiopia, the role of women is to take care of the family, so when they get sick, suffer disorders in their usual functions and care more about the family. In addition, concerns about the future of children are common in this country and may contribute to extol emotional aspects, above physical [54], even similar results were found in poor regions of Brazil [57].

However, in addition to previous studies not performing evaluations between chemotherapy cycles, making it impossible to verify changes during treatment, they also did not verify the specific influence of aspects drugs such as anthracycline drugs, as performed in our study, therefore, although our findings do not demonstrate changes in emotional aspects, the negative changes found in the FC domain are important to guide professionals on the use of resources in order to avoid or mitigate these changes, thus improving the quality of life of this population.

Additionally, despite the relevant findings of the present study, we can cite as a limitation the performance of evaluations only during one period of chemotherapy treatment, and the entire treatment process was not observed. Therefore, it is not possible to extrapolate the results to the complete treatment. In addition, adriamycin-based chemotherapeutic agents were used, and cannot be extrapolated to other types of chemotherapy.

Conclusions

Chemotherapy cycles with anthracyclines reduced the performance of SF, FC and muscle activation, as well as altered the levels of fatigue and quality of life, however, no effects on anxiety were observed. These results are important and innovative, being the first study to find these changes resulting only from the use of anthracyclines, which in most cases is linked to negative effects on the cardiovascular parameters.

Therefore, these results may contribute to the creation of strategies to improve the treatment of the disease. In addition, further research is needed to investigate the effects of other types of chemotherapy drugs on the variables analyzed.

Disclosure of conflict of interest

None.

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