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BREAST CANCER SURVIVORS HAVE LESS LEAN MASS AND LOWER PHASE ANGLE AFTER CANCER TREATMENT

Sobreviventes do câncer de mama tem menos massa magra e menor ângulo de fase após o tratamento oncológico

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ABSTRACT

Objective: To evaluate the weight status and body composition of women who survived breast cancer after cancer treatment. **Methods:** This is a before and after clinical study, in which 27 breast cancer survivors were evaluated before (T0) and after (T1) cancer treatment (surgical and clinical). Current weight and height were measured to determine the body mass index (BMI). Body composition was assessed by tetrapolar bioelectrical impedance. The percentage of fat and lean mass and the phase angle were calculated. We used Student's *t*-test to assess the difference among means of anthropometric variables and body composition between T0 and T1, and the McNemar's test to evaluate differences in the prevalence of overweight, adopting a 5% significance. **Results:** Patients have a mean increase of 2.6 kg in weight after treatment (p=0.00) and 1.15 km/m^2 in BMI (p=0.00). The percentage of fat mass increased by 0.6% (p=0.003) in T1, while the lean mass decreased (p=0.03). Concerning the phase angle, the mean decrease is 0.6 (p=0.026) after treatment. **Conclusion:** Breast cancer survivors have increased adiposity, decreased lean mass, and compromised cell integrity after cancer treatment, suggesting elevated risk factors for disease recurrence.

KEYWORDS: breast cancer; survivors; drug therapy; body composition.

RESUMO

Objetivo: Avaliar o estado do peso e a composição corporal de mulheres sobreviventes do câncer de mama após tratamento oncológico. **Metodologia:** Trata-se de estudo clínico do tipo antes e depois, em que 27 pacientes sobreviventes do câncer de mama foram avaliadas antes (T0) e depois (T1) do tratamento oncológico (cirúrgico e clínico). Aferiram-se peso atual e estatura para definição do índice de massa corporal (IMC). A avaliação da composição corporal deu-se por impedância bioelétrica tetrapolar, sendo aferidos percentual de massa gorda e de massa magra e ângulo de fase. Aplicou-se o teste *t* de Student para avaliar a diferença de médias das variáveis antropométricas e de composição corporal entre T0 e T1, bem como o teste de McNemar para avaliar diferenças na prevalência de sobrepeso, adotando significância de 5%. **Resultados:** As pacientes têm aumento médio de 2,6 kg após o tratamento (p=0,00) e 1,15 kg/m^2 no IMC (p=0,00). O percentual de massa gorda aumenta 0,6% (p=0,003) e há redução na massa magra (p=0,03) no T1. Em relação ao ângulo de fase, há diminuição média de 0,6 (p=0,026) após o tratamento. **Conclusão:** Mulheres sobreviventes do câncer de mama têm aumento de adiposidade, redução da massa magra e piora da integridade celular após o tratamento oncológico, o que sugere acréscimo de fatores de risco para recidiva da doença.

PALAVRAS-CHAVE: câncer de mama; sobreviventes; tratamento farmacológico; composição corporal.

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INTRODUCTION

Breast cancer is the most prevalent kind of neoplasm among women. It is considered a serious public health problem[1]. In 2012, the number of women diagnosed with breast cancer worldwide was 1.67 million, corresponding to 25% of all cancers[2]. According to an estimate from the International Agency for Research on Cancer (IARC)[3], there will be more than three million new cases and about 900,000 deaths from breast cancer in 2040. In Brazil, the epidemiological pattern is similar to that of the world, with the emergence of 57,900 cases of breast cancer among women being expected for the biennium 2018/2019. Among them, 11,800 will occur in the Northeast Region, representing 20.3% of all cases[1].

In parallel with the high incidence, breast cancer treatments have resulted in more effective outcomes, with a consequent increase in disease-free survival time[4]; however, important side effects are associated with antineoplastic therapies. Weight variation is a common condition during and after breast cancer treatment, and 50 to 96% of women in the early stage of the disease experience significant weight gain in this period. In addition to weight gain, breast cancer patients present unfavorable changes in body composition, with a significant increase in the percentage of adipose tissue and decreased lean body mass[5].

In this sense, body composition emerged as an important prognostic factor in cancer patients[6], because most of the adipose tissue is associated with the presence of chronic low-grade inflammation, with the consequent increase in cell proliferation and decrease in apoptosis[7]. Also, the smaller amount of muscle mass raises the risk of surgical complications and reduces quality of life and survival[8]. Despite the evidence, studies that assess the body composition of Brazilian women who survived breast cancer before and after cancer treatment are still scarce[9].

In this study, we hypothesize that breast cancer survivors gain weight and undergo changes in their body composition after cancer treatment, with increased fat mass and reduced lean mass. Thus, we aimed at evaluating the weight status and body composition of breast cancer survivors after cancer treatment.

METHODS

This is a before and after clinical study, conducted at Centro Regional Integrado de Oncologia (CRIO), in Fortaleza (CE), Brazil, with 27 patients diagnosed with breast cancer. Data were collected in two moments:

- T0: before the start of clinical treatment;
- T1: at the end of clinical treatment (chemotherapy or radiotherapy), between January 2010 and March 2011.

The study used a consecutive non-probabilistic convenience sample, and patients aged over 19 years and under 60 years, without previous clinical cancer treatment, were considered eligible.

Information about age, years of schooling, family income in minimum wages (MW), tumor location, clinical staging (CS), and type of clinical treatment performed (chemotherapy or chemotherapy + radiotherapy) was gathered by means of direct interview and search of medical records.

Current weight (CW), height, and body composition were considered and measured in moments T0 and T1 to establish the nutritional diagnosis. A Welmy® mechanical scale, with a capacity of 150.0 kg and precision of 100.0 g, was used to measure the CW. The stadiometer of the scale was used to measure the height. Body mass index (BMI) was calculated using the equation weight (kg)/height^2 (m) and evaluated according to the classification of the World Health Organization (WHO)[10]. Percentages of fat mass (%FM) and muscle mass (%MM) and the phase angle (PA) were obtained by bioelectrical impedance analysis (BIA) using the BIA 450e bioimpedance analyzer from Biodynamics®. The evaluation of the patients' %FM followed the Lohman classification[11], and the PA reference values followed the parameters described by Barbosa-Silva et al.[12].

Qualitative variables are presented as simple frequency and absolute numbers. Quantitative data are expressed as mean and standard deviation. The normality of the variables was verified using the Kolmogorov-Smirnov test to continue the evaluation of the difference in weight, BMI, %FM, %LM, and PA averages between moments T0 and T1. The normal distribution of the variables allowed the use of Student's *t*-test to compare the means. McNemar's test verified the difference in overweight prevalence between the two moments. All analyses used the Statistical Package for Social Sciences (SPSS), version 20.0, considering a 5% significance.

The Research Ethics Committee of the Universidade de Fortaleza (No. 359/2009) and CRIO approved this study. All participants were informed about the study and signed the informed consent form.

RESULTS

Patients had a mean age of 47 years (±6.6). Most had five or fewer years (62.9%) of schooling and a family income lower than three MW (77.8%). Regarding the clinical profile, all women had ductal carcinoma, and 25.9% were in CS III (Table 1). Out of the 27 patients evaluated at T0, 18 were assessed at T1. We lost three patients throughout the follow-up, as they refused to participate in T1, one who died, and five because we were not able to contact them again. The overweight prevalence (including obesity) was similar before (77.7%) and after treatment (83.3%) (p=0.50).

A significant weight increase (p=0.00) was present among women after cancer treatment, ranging from 0.4 to 4.8 kg, with a mean of 2.6 kg. BMI also showed a significant increase of 1.15 kg/m^2 (p=0.00) (Table 2).

Table 1. Description of socioeconomic and clinical characteristics and body mass index (BMI) status of patients.

Variable	n	%
Schooling		
<5 years	17	62.9
>5 years	10	36.1
Family income		
0–3 MW	21	77.8
>3 MW	6	22.2
Tumor location		
Ductal	27	100
Lobular	0	0
Clinical staging		
I	4	14.8
II	5	18.5
III	7	25.9
Not described*	11	40.8
BMI status†		
Moment T0		
Normal weight	6	22.3
Overweight**	21	77.7
Moment T1§		
Normal weight	3	16.7
Overweight**	15	83.3

MW: Minimum wage (MW in 2010: R$ 510/MW in 2011: R$ 545); BMI: body mass index; T0: before the first cycle of chemotherapy; T1: end of the last cycle of chemotherapy and/or radiotherapy; *information not described in the medical records; **overweight and obesity; §only 18 women were reevaluated at T1; †McNemar's Test: difference between the prevalence of overweight at T0 and T1 (p=0.50).

Table 2. Weight, body mass index (BMI), and body composition status at moments T0 and T1.

Variable	Moment of evaluation	Values	p
Current weight	T0	66.6	0.00*
	T1	69.2	
BMI	T0	28.4	0.00*
	T1	29.5	
%LM	T0	65.3	0.03*
	T1	64.5	
%FM	T0	34.7	0.04*
	T1	35.3	
PA	T0	6.6	0.026*
	T1	6.0	

T0: before the first cycle of chemotherapy; T1: end of the last cycle of chemotherapy and/or radiotherapy; %LM: lean mass percentage; %FM: fat mass percentage; PA: phase angle; *Student's *t*-test (p<0.05).

Evaluating body composition, we found a significant reduction in %LM (p=0.03) and PA (p=0.026) and a significant increase in %FM (p=0.04) after cancer treatment (Table 2).

DISCUSSION

This study aimed to evaluate the body composition of breast cancer survivors after cancer treatment and show that patients have an increase in %FM and a reduction in %LM and PA. Also, an important weight and BMI increase stood out after clinical antineoplastic treatment. These findings reveal a worrying scenario among breast cancer survivors living in Northeastern Brazil, given the presence of adiposity, clearly described as a risk factor for disease recurrence[13] because of the numerous metabolic changes triggered by the state of chronic low-grade inflammation[14].

Weight gain during chemotherapy treatment can range from 2.5 to 6.2 kg, and gains of more than 10 kg[15] are not uncommon. This condition has been reported in the literature since 1985, when Heasman et al.[16] revealed this change in women with breast cancer for the first time. Our group has previously described this condition in patients living in the Southeast Region of Brazil, who, after three months of chemotherapy treatment, presented an average weight gain of 3 kg and an increase of 1 kg/m^2 in BMI[9]. However, in the Northeast Region, socioeconomic conditions are very different, especially in relation to income and schooling, aspects that greatly interfere in the nutritional status of individuals. The region has the highest prevalence of inadequate macro and micronutrient intake[17] in Brazil according to results from the survey *Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico* (Vigitel),[18] which indicate that the increase in overweight and obesity among Brazilian women is greater in those with lower levels of education. Thus, the findings of the present study fill this gap in the national literature concerning weight status and body composition of Northeastern women who survived cancer. In addition, they answer a call from the third report of the World Cancer Research Fund (WCRF)[19] entitled *Diet, Nutrition, Physical Activity and Cancer: a Global Perspective,* which indicates the lack of studies that assess diet, nutrition, and physical activity in cancer patients from low-income countries.

The causes for weight gain after breast cancer diagnosis are unclear; however, they might involve changes in the woman's energy metabolism, including reduced basal metabolic rate, decreased physical activity and thermogenesis, and increased food intake[20]. In our study, weight gain ranged from 0.8 to 4.8 kg, and more than 80% of patients showed overweight after treatment. This result is similar to that found by Yeo et al.[21], who evaluated women with breast cancer and found that 52.1% of patients reached a BMI corresponding to overweight/obesity. This condition of weight gain and change in nutritional status has been widely discussed[6], especially when it comes to weight gain in adulthood[22], notably

recognized as a risk factor for breast cancer. However, weight gain in surviving women, which begins during cancer treatment, needs to be seen as a risk factor for recurrence, lower survival, and worse quality of life for these patients. Some authors have recognized[23] the value of providing guidance on lifestyle modification for these patients in order to minimize weight gain and ensure a better prognosis, given the importance of understanding that self-care affects patient survival.

Several mechanisms seek to explain the relationship between obesity and the worse prognosis for breast cancer patients, and all of them converge on endocrine and metabolic changes promoted by excess adipose tissue[24]. This fact has been attributed, in part, to the high levels of circulating estrogen caused by the increased expression of aromatase, stimulated by the high percentages of adipose tissue, and also due to the presence of inflammatory mediators chronically released by this tissue. Among these mediators, tumor necrosis factor α (TNF-α) and interleukin-6 (IL-6) act by stimulating the cell cycle and inhibiting apoptosis, which contributes to tumor progression[24].

In addition, insulin, insulin-like growth factor (IGF-1), and leptin increase in the presence of obesity and favor breast carcinogenesis[14]. Insulin indirectly influences cancer growth and metastatic potential, because the rise in its levels promotes synthesis and intensifies IGF-1 activity. In turn, IGF-1 is involved in regulating the growth, survival, and differentiation of neoplastic cells and, together with other growth factors, can act synergistically to increase the mitogenic potential of these cells[13]. Similarly to insulin and IGF-1, leptin plays pro-carcinogenic roles, such as stimulation of normal and tumor cell growth, cell migration and invasion, and enhancement of angiogenesis, which suggest its direct relationship with an aggressive type of breast cancer or its participation in increasing tumor aggressiveness with a higher chance of metastasis[14].

Thus, the importance of knowing, besides weight and BMI, the body composition of these patients becomes clear, given the evidence of a change in body composition after the diagnosis and treatment of breast cancer, with increased adipose tissue and reduced lean tissue, leading to the development of sarcopenic obesity[25]. Women evaluated in this study presented reduced lean mass and increased fat mass after cancer treatment, corroborating the results by Cisneros et al.[26], in which women with the same cancer diagnosis had increased fat mass and reduced lean mass after chemotherapy.

In addition to excess fat, the reduction in lean mass identified in the patients evaluated also needs attention. Literature has shown an association between lower muscle mass and the diagnosis for a variety of cancer types, including breast cancer. Also, this decrease in muscle mass raises the risk of surgical complications and reduces quality of life and survival[9]. Mazzuca et al. [27] identified %LM below the desired in women with breast cancer soon after diagnosis, and that this percentage continued to drop after cancer treatment, corroborating our results. Individuals with less lean mass should receive higher doses of chemotherapy per unit of body weight, which may lead to greater treatment toxicity. Besides, recent studies attest to deleterious effects caused by the loss of lean mass in breast cancer patients, resulting in longer hospital stay, toxicity, and mortality[6].

In addition to fat and lean mass, PA has been described as an important predictor of clinical prognosis among body composition parameters. It is understood as a marker of cell integrity and cell membranes that attributes a functional status to these structures. Low PA suggests cell death or decreased cell integrity, while higher PA indicates healthy cell membrane[28]. Thus, low PA values point to changes in cell integrity, which, in cancer patients, may be associated with worse prognosis, lower survival, and quality of life impairment[28].

In this study, patients had lower PA after chemotherapy, which may indicate a worse prognosis. According to Gupta et al.[29], who investigated PA as an indicator of the prognosis for breast cancer, the mean PA score in these patients was 5.6 (1.5–8.9). Those with PA≤5.6 had a median survival of 23.1 months, while patients with a value >5.6 had survival of 49.9 months. The difference is statistically significant (p=0.031), associating PA with survival. In our study, the mean PA value was 6.6 at T0 and 6.0 at T1, both higher than those presented in the literature; however, we underline the significant reduction after cancer treatment and that this measure can be a potential marker of clinical prognosis.

We emphasize an important limitation of the present study, which concerns the number of patients evaluated, considering the high prevalence of breast cancer. However, we highlight that this study presents significant results regarding cancer survivors, a population still little studied in our country, especially in the Northeast Region. In addition, these patients were selected in a reference cancer center in the state that treats people with low socioeconomic status. Therefore, they experience social vulnerability factors that favor the late diagnosis of the disease, lack of follow-up after treatment, and exposure to a higher risk of recurrence and lower survival rate.

Thus, the assessment of these patients, knowing the possible changes in weight, nutritional status, and, mainly, body composition, allows targeting health actions to this public to minimize risk factors related to lifestyle and help to prevent recurrence. Besides, this study has a significant follow-up time of patients, which strengthens the findings presented. We also filled a gap in the national and international literature concerning the evaluation of cancer patients in different regions of Brazil, contributing to expand the knowledge about patients from low- and middle-income countries.

CONCLUSION

The breast cancer survivors evaluated had their body composition changed after cancer treatment, with reduced lean mass and

increased fat mass. They also presented a significant weight gain and a rise in BMI, factors suggestive of higher risk of recurrence among women already diagnosed with more advanced tumors. In addition, PA decreases during treatment, which indicates a change in cell integrity, culminating in another factor suggestive of a worse prognosis. Thus, we recommend evaluating nutritional status and body composition at the time of diagnosis of breast cancer and including direct and individualized nutritional guidance after diagnosis. These strategies can minimize weight gain and changes in body composition in clinical practice, besides contributing to a better prognosis, survival, and quality of life among breast cancer survivors.

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