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The influence of body composition on quality of life of patients with breast cancer

Aline Porciúncula Frenzel[1], Carla Aberici Pastore[2] and Maria Cristina González[1,2]

[1]Post-Graduation Program in Nutrition and Food. Federal University of Pelotas. Brazil. [2]Post-Graduation Program on Health and Behavior. Catholic University of Pelotas. Brazil.

Abstract

Introduction: **Unwanted changes in body composition, as well as their impact on these people's quality of life, have been little investigated in patients with breast cancer.**

Objetive: **To assess the role of body composition on quality of life and the impact of chemotherapy on both, in women with breast cancer.**

Methods: **It was assessed prospectively women with breast cancer in a cohort of patients undergoing chemotherapy. Body composition was estimated through bioelectrical impedance. The quality of life was evaluated using the World Health Organization quality of life questionnaire.**

Results: **This study assessed 70 women, 77 and 73% of those were initially overweight and had excess of body fat, respectively. There was a significant increase in fat-free mass (p > 0.001), body mass index (p = 0.03) and weight (p = 0.02) while quality of life stayed the same during the study. Moreover, women with excess of body fat showed a significantly lower initial general health score, compared to those with normal body fat (p = 0.02).**

Conclusions: **Chemotherapy proved to be a potential inducer in the weight gain in this population. We highlight the importance of further investigation about the impact of body fat accumulation on those women's quality of life.**

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Key words: *Body composition. Breast cancer. Quality of life. Obesity. Sarcopenia.*

INFLUENCIA DE LA COMPOSICIÓN CORPORAL EN LA CALIDAD DE VIDA DE LOS PACIENTES CON CÁNCER DE MAMA

Resumen

Introducción: **Los cambios no deseados en la composición corporal, así como el impacto de éstos en la calidad de vida de esta población, han sido poco investigados.**

Objetivo: **Evaluar el rol de la composición corporal en la calidad de vida, y el impacto de la quimioterapia en ambos, en mujeres con cáncer de mama.**

Métodos: **Se evaluaron prospectivamente las mujeres con cáncer de mama en una cohorte de pacientes sometidos a quimioterapia. La composición corporal se estimó mediante la impedancia bioeléctrica. La calidad de vida se evaluó mediante el cuestionario de calidad de vida de la Organización Mundial de la Salud.**

Resultados: **Se evaluaron 70 mujeres, de las cuales el 77 y 73% tuvieron inicialmente sobrepeso y exceso de grasa corporal, respectivamente. Se observó un aumento significativo en la masa libre de grasa (p < 0,001), el índice de masa corporal (P = 0,03) y el peso (p = 0,02), mientras que la calidad de vida se mantuvo igual durante el período. Por otra parte, las mujeres con exceso de grasa corporal, mostraron una puntuación general de salud inicial significativamente menor, en comparación con aquellas con grasa corporal normal (p = 0,02).**

Conclusiones: **La quimioterapia ha demostrado ser un inductor potencial del incremento de peso en esta población. Destacamos la importancia de nuevas investigaciones sobre el impacto de la acumulación de grasa corporal en la calidad de vida de estas mujeres.**

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Palabras clave: *Composición corporal. Cáncer de mama. Calidad de vida. Obesidad. Sarcopenia.*

Correspondence: Aline Porciúncula Frenzel.
post-Graduation Program in Nutrition and Food.
Federal University of Pelotas.
R. Coronel Alberto Rosa, 403, Centro.
CEP 96010-770 Pelotas. RS. Brazil.
E-mail: aline.frenzel@hotmail.com

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Abbreviations

FMI: Fat Mass Index.
FFMI: Fat Free Mass Index.
WHOQOL-bref: Brief version of the Instrument for Assessment of the Quality of Life of the World Health Organization.

Introduction

According to the International Agency for Research on Cancer (World Cancer Report, 2008), the overall impact on cancer has more than doubled over the last 30 years. Among tumors with higher incidence in females, both in developed and developing countries, is breast cancer. In Brazil, not only is breast cancer considered to be with the highest incidence among women, but it also shows high mortality rates.

In addition to cancer diagnosis, the interaction between nutritional status, body composition and factors related to treatment represent a complex combination which can dictate the quality of life of cancer patients.

From the patient's perspective, the measurement of quality of life in women with breast cancer presents itself as an important resource to evaluate the treatment results. Quality of life can be defined as one's subjective perception of their inability and of their satisfaction with their current level of functionality. Recent studies have shown that quality of life of women with breast cancer is positively associated with the clinical outcome and tolerance to the antineoplastic treatment.

Increase in the Body Mass Index (BMI) after the diagnosis of breast cancer and the high prevalence of overweight and obesity in this population have been quite highlighted. Furthermore, current evidence suggests that women undergoing chemotherapy may show metabolic changes in skeletal muscle. This effect, possibly caused by the action of some chemotherapy drugs, seems to lead to a decrease of the muscle mass and strength.

Despite the increasing knowledge about the consequences of nutritional disorders, especially in patients with cancer, these changes are most of the times underdiagnosed. The lack of recurrent use of methods which allow the evaluation of body composition and nutritional status may be a reason for this problem.

Bioelectrical impedance analysis (BIA) is a commonly used method for estimating body composition, which allows to evaluate muscle mass and body fat, as well as their changes. This method has been proved to be one of the best alternatives in clinical practice, because it is considered fast, relatively accurate, easy to perform, reliable and noninvasive. Moreover, BIA can be applied at the bedside.

Considering the aspects mentioned above, we see the importance of evaluating body composition in patients with breast cancer and its impact on quality of life of this population. Obtaining these data may provide subsidy for assessing therapeutic tolerance and appropriate choice of the clinical and nutritional therapy. Therefore, the aim of this study was to assess the role of body composition on quality of life in a subsample of women with breast cancer, belonging to a cohort of patients undergoing chemotherapy. In addition, we sought to investigate the impact of chemotherapy on these women's quality of life and body composition.

Methodology

This study comprises a snippet from a longitudinal study, which evaluated prospectively all patients aged 18 or over, who started chemotherapy at the Teaching Hospital of the Federal University of Pelotas from March 2004 to July 2005. Thus, we used a subsample of the initial study, consisting of all women with breast cancer who took part in the study and were followed up until the fourth cycle of chemotherapy or more.

The Ethics Committee of Federal University of Pelotas approved the research. The informed consent form was signed by the patient on the day of his or her first chemotherapy application.

Data concerning chemotherapy indication and stage of disease were obtained from the patient's electronic record.

To perform the anthropometric assessment (from the collection of height and weight) and the body composition (using BIA) patients were instructed to be fasted. These measures, except height (measured only once), were collected in the beginning and in the end of each chemotherapy cycle. In the present study we used anthropometric and body composition data collected in the beginning of the first and last chemotherapy cycles.

To measure weight it was used a digital Filizola™ scale model PL 150 with a capacity for 150 kg and accuracy of 100 g. The height measure was done using a anthropometer of 200 cm and accuracy of 1 mm, linked to the scale.

The BIA was done using a BIA Quantum tool (RJL Systems™), with frequency of 50kHz, according to standardized technique. Three values of resistance and reactance were obtained, having taken the highest value of three measures of both parameters, which were used for subsequent estimation of body composition (fat free mass and body fat) through the V Corp™ program.

To assess the nutritional status, the BMI was calculated, obtained by dividing the weight (in kilos) by the square of height (in meters), being presented according to the World Health Organization classification (underweight: BMI < 18.5 kg/m^2, appropriate: BMI between 18.5 and 24.9 kg/m^2; overweight: BMI between 25.0 and 29.9 kg/m^2 and obesity: BMI ≥ 30 kg/m^2).

The criteria proposed by Kyle was used as a reference to classify the women regarding body composition. This classification is given by cutoff points for fat mass index (FMI-kg/m^2) and fat free mass index (FFMI-kg/m^2), according to the gender. These rates were obtained from the data of BIA and the patients'

Table I
WHOQOL-bref domains and general questions scores in the first and last cycle of chemotherapy of a sample of breast cancer women (n = 70)

WHOQOL domains	*Average (or median) e SD (or IQI)*[c]		*p*[a]
	First cycle	*Last cycle*	
Physical	64.3 (IQI: 63.5; 75.0)	67.9 (IQI: 53.6; 78.6)	0.75
Psychological[b]	68.5 ± 14.9	69.7 ± 12.6	0.60
Social Relations	76.1 ± 13.0	74.3 ± 15.0	0.40
Environment[b]	65.6 (IQI: 56.3; 71.9)	64.1 (IQI: 53.1; 71.9)	0.08
General questions			
Overall Quality of life	18.3 ± 4.0	17.6 ± 6.3	0.32
General Health	14.9 ± 5.1	15.5 ± 6.8	0.42

[a]t test or Wilcoxon.
[b]n < 70.
[c]SD: Standard deviation; IQI: Inter-Quartile Interval.

height. Thus, the patients could present: muscle mass deficiency (FFMI ≤ 15 kg/m^2) or normal muscle mass (FFMI > 15 kg/m^2) and excess of body fat (FMI ≥ 8.2 kg/m^2) or normal body fat (FMI < 8.2 kg/m^2).

Quality of life was evaluated using the WHOQOL-bref tool, short version in Portuguese of the World Health Organization Quality of Life Assessment-WHO. This instrument consists in 26 questions divided into four domains: physical, psychological, social and environment. Moreover, it presents two general questions of quality of life (general quality of life and general health). The answers to all those questions were collected through a Likert scale, with scores ranging from 1 to 5, later being transformed into a scale from 0 to 100, so that higher scores were related to better quality of life.

The WHOQOL-bref questionnaire application occurred in two stages: in the first 72 hours of the first cycle and repeated in the last 72 hours of the last cycle.

Statistical analyses were performed using the statistical package Stata 11.0™. The variables were evaluated regarding their normal distribution. The average values and standard deviation or median and interquartile range, from variables with and without normal distribution, respectively, allowed their descriptive analysis. The Wilcoxon or paired student's t-test enabled the comparison between the initial and final values (first and last+ chemotherapy cycles) of BMI, FFMI, FMI and of each domain and general question of the WHOQOL-bref. To compare the several aspects of WHOQOL-bref among patients with excess of body fat and with normal body fat, the student's t-test or Mann-Whitney test were used. For all tests, a value of $p < 0.05$ was considered significant.

Results

Out of 191 patients who started chemotherapy treatment at the Teaching Hospital of Federal University of Pelotas, from March 2004 to July 2005, and who agreed to take part in this study, 73 were diagnosed with breast cancer, being all women. Two of them stopped the treatment before the fourth chemotherapy cycle, one of the interruptions because of death. Thus, 71 women were assessed until the fourth chemotherapy cycle or more, of which 56 were followed during six to eight cycles and 15 during four to five cycles. One patient did not answer the WHOQOL-bref questionnaire in the last cycle. So, the sample of the present study consisted of 70 women.

The patients' average age was of 55.6 ± 11.3 years, 90% of them were 40 years old or more.

As characteristics of the disease, the majority of women were in stage II (77%) and were under neoadjuvant or adjuvant chemotherapy treatment (94%).

Table I presents the average score of each domain and general questions of the questionnaire WHOQOL-bref applied in the first and last chemotherapy cycles. The results show that there was no significant difference ($p \geq 0.05$) in any domain or general question of the quality of life assessment between the beginning and end of the chemotherapy, showing no effect of this treatment on this aspect.

The patients' average weight was significantly higher ($p = 0.02$) at the end of the treatment when compared to the beginning (70.2 ± 14.3 kg and 69.4 ± 13.6 kg, respectively). However, when they were grouped according to the BMI, there was a significant increase in weight only in those women who started the chemotherapy treatment with BMI ≥ 25 kg/m^2 ($p = 0.02$). The average height of this sample was of 1.54 ± 0.06 m.

The nutritional assessment by BMI showed that 23% and 21.4% of women had this index within the regular standards at the beginning and at the end of chemotherapy, respectively. It was also observed that five women (7.1%) presented a higher BMI at the end of the treatment (table II). Because no woman had BMI under 18.5 kg/m^2 at the first and last cycle, this gap was not expressed in the table.

Table II
Classification by BMI, FMI and FFM, at the beginning and at the end of chemotherapy, of a sample of breast cancer women (n = 70)

Index	*n (%) initial*	*n (%) Final*
BMI[a] (kg/m²)		
18.5-24.9	16 (22.8)	15 (21.4)
25-29.9	27 (38.6)	26 (37.2)
≥ 30	27 (38.6)	29 (41.4)
FFMI[b] (kg/m²)		
> 15	69 (98.6)	69 (98.6)
≤15	1 (1.4)	1 (1.4)
FMI[c] (kg/m²)		
≥ 8.2	51 (72.9)	51 (72.9)
< 8.2	19 (27.1)	19 (27.1)

[a]Body mass index.
[b]Fat free mass index.
[c]Fat mass index.

Concerning the FMI, 51 women (72.9%) had this index above the normal standards established in this study, while only one woman had FFMI ≤ 15 kg/m² (1.4%). These results were identical at the first and at the last chemotherapy cycle. Thus, only 18 women (25.7%) had normal body composition in the beginning and in the end of the analysis.

In order to identify changes in body composition and nutritional status between the beginning and the end of the chemotherapy treatment, it was made an analysis comparing initial and final FMI, FFMI and BMI. The results showed that the patients presented a significant increase in BMI (0.34 kg/m², p = 0.03) and FFMI (0.36 kg/m², p < 0.001) during the treatment. However, there was no significant change in FMI (fig. 1).

The fact that only one woman presented lack of muscle tissue at the beginning, as well as at the end of the treatment (FFMI ≤ 15 kg/m²), did not make it possible to evaluate its impact on the different aspects of quality of life of the sample studied.

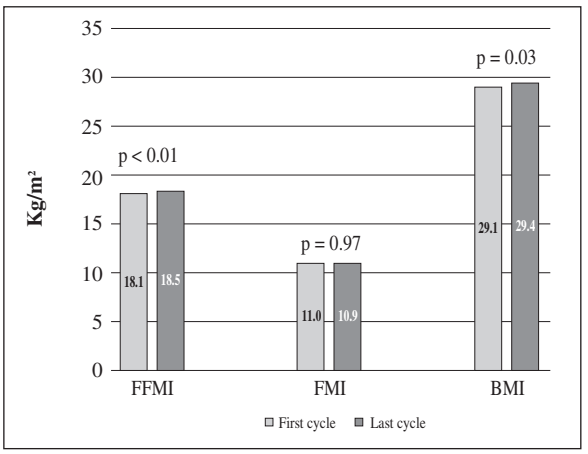


Fig. 1.—Average Fat Mass Index (FMI), Fat Free Mass Index (FFMI) and Body Mass Index (BMI) in the first and last cycle of chemotherapy (n = 70).

However, when compared quality of life of women with excess of body fat and with normal body fat (fig. 2), according to FMI, it was found a significant difference in the average score of general health in the beginning of the treatment. It was observed that women with body fat excess showed significantly lower average score in these domains when compared to those with normal body fat. Although no significant difference was found in other domains and general questions of quality of life (among patients with FMI ≥ 8.2 kg/m² and FMI < 8.2 kg/m²), the average of all of them (except the final physical domain) was lower for women with excess of body fat.

Discussion

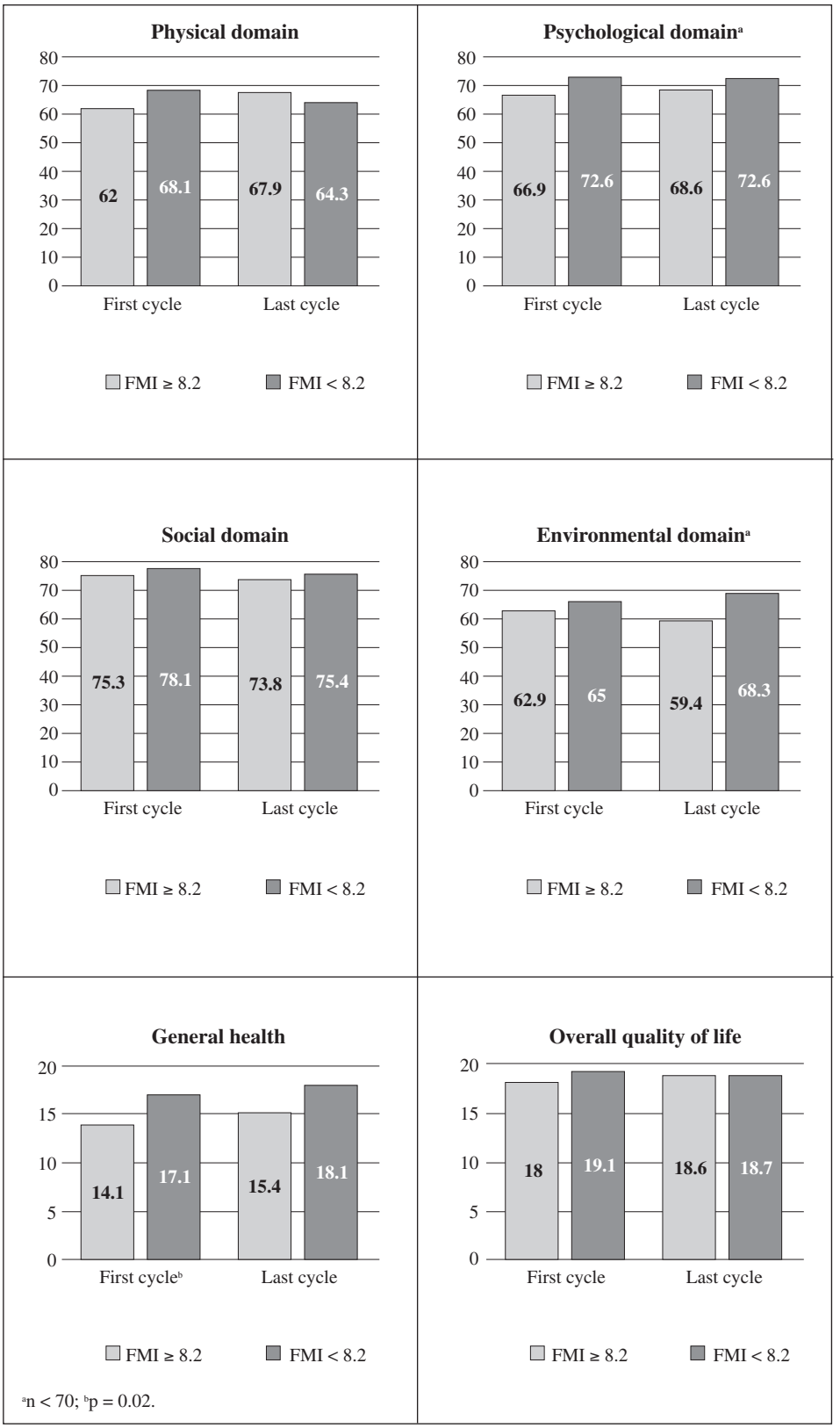
The present study aimed to show the influence of body composition on quality of life, as well as the impact of chemotherapy on both, in a sample of women with breast cancer belonging to a cohort of patients undergoing chemotherapy.

Although Brazil still has high mortality rates because of breast cancer, advances in diagnosis and therapy have allowed to identify the disease in early stages and to apply more specific antineoplastic treatment. In this sense, the number of survivors, as well as life expectancy, has increased after the diagnosis. The results of this study are in agreement with these findings, in which most of the women was in stage II of the disease and only one death was registered during the analysis of the patients. Therefore, it has been given special attention to the decrease of risk of tumor recurrence, the promotion of disease-free survival and the increase of quality of life in patients with breast cancer.

The quality of life evaluation has been used, within the health care, as an important tool to measure the impact of the disease on the patient's scope, enabling to create indicators of the severity and progression of the disease, as well as predictors of the treatment influence on the patient's health conditions.

The implementation of QOL assessments into clinical practice for breast cancer treatment has a high potential to benefit patients. Health-related quality of life has increasingly been an important factor to consider in the holistic treatment of these patients and, by providing accurate insights into QOL through self-reported questionnaires, physicians will be better able to make treatment decisions.

In this study, based on the various dimensions of quality of life assessed, there were no changes in any of them between the beginning and the end of chemotherapy treatment. Rebelo et al found a protective effect of older age on quality of life of women with breast cancer. This possible association may explain the results of this study, in which only 10% of women were



[a]n < 70; [b]p = 0.02.

Fig. 2.—Quality of life scores and Fat Mass Index (FMI) in women undergoing chemotherapy for breast cancer (n = 70).

under 40 years old and no change on quality of life after chemotherapy was observed. It should yet be considered that this study did not suffer survival bias which could explain the absence of changes on quality of life, since from the three losses, only one was because of death.

On the other hand, one limitation to be considered in this study refers to the kind of questionnaire used to

assess quality of life. It was chosen to use a generic questionnaire to measure this variable. This was because, when designing the initial study, the valid translation of the European Organization for Research and Treatment of Cancer questionnaire (EORTC QLQ C-30) was not available. Nevertheless, we should highlight that the WHOQOL-bref originated from a scientific and multicenter study, legitimated by the WHO. Moreover, the development and validation of the Portuguese version of this questionnaire followed strict scientific and ethnic criteria.

The prevalence of initial weight excess (overweight and obesity) of 77% and the average BMI (29.1 kg/m^2) of women studied in the beginning of chemotherapy treatment support the literature data, concerning the role of weight excess to the risk of developing breast cancer. Furthermore, the fact that approximately 73% of women had excess of body fat in the beginning of chemotherapy suggests that, besides weight excess, the increase in adipose tissue may also be associated with the development of this kind of neoplasm. Studies have also shown that women with breast cancer who are overweighed or obese and who present some alteration in their body composition have a worse prognosis and a higher risk of tumor recurrence.

The significant increase in weight and BMI observed in this sample confirms the other literature data. Demark evaluated 53 women with breast cancer within the first three weeks and one year later the diagnosis and noticed a higher average gain in total weight among those women who were undergoing chemotherapy when compared to the others. Similarly, Voskuil found that chemotherapy treatment in patients with breast cancer seems to induce weight gain. Still in agreement with these findings, it was possible to observe in this sample that five women (7.1%) went to a higher category of BMI classification during chemotherapy treatment.

According to Aslani, the weight gain in women with breast cancer undergoing chemotherapy treatment is mainly due to the increase in total body water and adipose tissue. However, Nissen noticed that women with breast cancer who have normal BMI in the diagnosis tend to gain more weight and body fat during chemotherapy, when compared to those with overweight or obesity. Opposed to this finding, in the present study the significant increase in weight occurred only in the group which started chemotherapy treatment with BMI ≥ 25 kg/m^2. Nevertheless, the maintenance of body fat observed in this sample during the analysis may be explained by Nissen's study.

In literature there are several explanations for the increase in weight in women with breast cancer undergoing chemotherapy. One of them is related to the combined action of drugs used in the treatment, like doxorubicin, adriamycin and corticosteroids. Concurrent use of these drugs contributes to a greater weight gain in women undergoing chemotherapy, when compared to those undergoing radiotherapy or surgery. However, drugs which promote isolation weight gain and water retention, such as tamoxifen and aromatase inhibitors were not included in chemotherapy protocols of the sample.

Demark, using the DEXA (Dual Energy X-ray Absorptiometry), observed an increase in adipose tissue and a likely decrease in muscle mass in women with breast cancer undergoing chemotherapy after one year of treatment. Studies also suggest that muscle mass can remain unchanged or show a decrease after chemotherapy treatment.

Unlike Demark's finding, in this study chemotherapy did not lead to a decrease in muscle mass, it was actually observed a significant increase in it. This meeting may be a justification for the maintenance of quality of life presented in the sample during treatment. However, the rating of body composition provided by BIA should be considered as a second limitation of this study. This method assess muscle mass by estimating body water. Thus, patients who show hydroelectrolytic alteration during BIA may have had their FFMI overestimated. Besides, because of the fact that body fat assessment is given by the difference of muscle mass, this limitation may have led to underestimation of body fat of the women studied.

Several authors suggest that chemotherapy induces to unusual weight gain, with an increase in adipose tissue in isolation. Martins et al. compared the body composition of patients with recent breast cancer diagnosis with women with benign breast alterations using BIA and observed that those with breast cancer showed higher values of body fat, with a statistically significant difference. These results confirm the present study, in which 73% of women showed excess of body fat when classified by FMI in the beginning of chemotherapy treatment.

So, the findings show that the initial weight excess and its increase during chemotherapy plus the initial changes in body composition should be considered situations which require some intervention. This is because, besides predisposing the development of breast cancer, the decrease in life expectancy and the increase in tumor recurrence, unwanted changes in weight and body composition raise the risk of developing other chronic non-communicable diseases, which can influence on those women's quality of life.

Another finding in this study was a tendency to lower quality of life scores in women with excess of body fat when compared to those with normal FFMI. This piece of information deserves further investigation, since it was not found in literature any other publication which addressed this association. Nevertheless, the increase in body weight after the start of treatment, the highlights sustainable of the impact of this gain on reduced quality of life, added to the fact that this gain occurs possibly at the expense of body fat, highlight the probable association between body fat and quality of life. However, must consider that this trend occurred

only at the beginning of treatment, showing that chemotherapy may have reduced the protective effect of body composition on the quality of life.

Therefore, we can conclude that it was not possible to show a significant impact of chemotherapy on quality of life of the women studied. Similarly, it was not possible to demonstrate clearly the influence of chemotherapy on body composition or the influence of body composition on quality of life. The lack of power, due to the limited sample size, may justify the absence of statistical significance in most of the analyses, especially when the sample was stratified to assess the impact of excess of body fat on quality of life.

Nevertheless, the plausible relationship between quality of life and body composition and the restricted literature addressing this issue in women with breast cancer shows the need for further studies in this area. This will allow a better understanding about this possible relationship, affording the development of strategies with a benefic effect in many health aspects and on quality of life of women suffering from breast cancer. These strategies must focus mainly in the acquisition of healthy eating habits and in the regular practice of physical activity. This is because, besides acting directly on the nutritional status and body composition, these practices may also contribute to the quality of life of women with breast cancer, who commonly have a long lifespan.

The impact of reducing the weight excess, especially associated with body fat accumulation, on prevention, decrease in recurrences and higher life expectancy of breast cancer have been quite highlighted in literature. The suggestion that excess of body fat may also influence on those women's quality of life increases the importance of control and intervention of these diseases in public health.

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Authors' contribution:

A.P.F.: Responsible for processing and analyzing data and writing the article.

C.A.P.: Collaborated in analyzing data and writing the article.

M.C.G.: Founder and responsible for coordinating the study, collaborated in analyzing data and writing the article.

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