## Nutrición Hospitalaria

# Original Dietary intake and oxidative stress in breast cancer: before and after treatments

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#### Abstract

*Objective:* The aim of this study was to investigate changes in dietary intake, anthropometric parameters and markers of oxidative stress in 40 women who underwent surgery, chemotherapy or radiation therapy for breast cancer.

Methods: Pretreatment and post-treatment measurements included data collected through a food frequency questionnaire, weight and height to calculate the body mass index (BMI) and oxidative stress markers assessed from blood reduced glutathione (GSH), serum antioxidant capacity (AC), plasma thiobarbituric acid reactive substances (TBARS), serum lipid hydroperoxides (LH) and plasma carbonyls. Differences were compared using paired Student's *t*-test or paired Wilcoxon's test.

**Results:** A significant increase (P < 0.05) in the intake of the food groups: meat and eggs, dairy products, beans, oils and fats, as well as food from the subgroups: red meat, milk and other dairy products rich in fat, fruit rich in vitamin C and vegetable fats was found after treatments. There was a significant increase in body weight (P < 0.05), BMI (P < 0.05), levels of TBARS (P < 0.0001), LH (P < 0.005) and carbonyls (P < 0.0001) and a significant decrease of levels of AC (P < 0.005) and GSH (P < 0.0001).

*Conclusion:* Breast cancer diagnosis and treatments were associated with dietary intake changes and increased body weight, BMI and oxidative stress. These potential changes have important implications for preventive nutrition counseling.

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Key words: Breast cancer. Dietary intake. Anthropometric parameters. Oxidative stress. Treatment.

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#### INGESTIÓN DIETÉTICA Y ESTRÉS OXIDATIVO EN CÁNCER DE MAMA: ANTES Y DESPUÉS DEL TRATAMIENTO

#### Resumen

*Objetivo:* El propósito de este estudio fue investigar los cambios en la ingesta dietética, los parámetros antropométricos y los marcadores del estrés oxidativo en 40 mujeres sometidas a cirugía, quimioterapia o radioterapia por cáncer de mama.

*Métodos:* Los datos recogidos antes y después del tratamiento fueron un cuestionario de frecuencia de consumo de alimentos, el peso y la talla para calcular el índice de masa corporal (IMC) y los marcadores de estrés oxidativo evaluados mediante el glutatión reducido (GSH) en sangre, la capacidad antioxidante sérica (CA), las sustancias reactivas del ácido tiobarbitúrico en el plasma (SRAT), los hidroperóxidos lipídicos (HPL) séricos y los carbonilos plasmáticos. Se compararon las diferencias usando la prueba t de Student o la prueba pareada de Wilcoxon.

**Resultados:** Después de los tratamientos se halló un aumento significativo (P < 0,05) en el consumo de los grupos de alimentos: carne y huevos, lácteos, legumbres, aceites y grasas, así como de los subgrupos: carnes rojas, leche y otros lácteos ricos en grasas, fruta rica en vitamina C y grasas vegetales. Hubo un aumento significativo en el peso corporal (P < 0,05), el IMC (P < 0,05), las concentraciones de SRAT (P < 0,0001), HPL (P < 0,005) y carbonilos (P < 0,0001) y un descenso significativo de la CA (P < 0,005) y de GSH (P < 0,0001).

*Conclusión:* El diagnóstico de cáncer de mama y sus tratamientos se asociaron con cambios en la ingesta dietética y un aumento del peso corporal, el IMC y el estrés oxidativo. Estos cambios potenciales tienen implicaciones importantes para el consejo sobre nutrición preventiva.

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Palabras clave: Cáncer de mama. Ingesta dietética. Parámetros antropométricos. Estrés oxidativo. Tratamiento.

## Abbreviations

AC: Antioxidant capacity. BMI: Body mass index. GSH: Reduced glutathione. LH: Lipid hydroperoxides. TBARS: Thiobarbituric acid reactive substances. FFQ: Food frequency questionnaire.

### Introduction

Breast cancer is one of the most important public health problems due to its growing incidence and mortality rates. In all over the world, breast cancer is considered the most frequent type of cancer among women. Every year, breast cancer accounts for 22% of new cancers found in women. In Brazil, 49.240 new breast cancer cases were expected for 2010, with an estimated risk of 49 cases per 100.000 women. For the Santa Catarina State, in southern Brazil, 1.570 new breast cancer cases were expected for 2010, with an estimated risk of 50 cases per 100.000 women. In spite of its high incidence, breast cancer can be considered a disease with a good prognosis if an early diagnose and appropriate treatment are done. The estimated average survival after five years of breast cancer is approximately 61%.1

Breast cancer is a disease with multiple etiological factors linked to genetic, environmental, social demographic, behavioral, psychological and hormonal factors.<sup>24</sup> Of the risk factors, nutritional factors can be associated to 30-40% of disease cases.5 In the recent decades, researches has studied the relationship between nutritional and life style factors and the development and/or progression of breast cancer. Original studies and literature reviews were carried out to clarify which elements in the diet could play a protective or determining role in the disease5-9, as well as the mechanisms through which nutrients could be involved in the progression, recurrence or mortality from breast cancer.<sup>10-11</sup> Additionally, nutritional factors might be directly related to the generation of reactive oxygen species in the body, triggering oxidative stress, causing cell oxidative damage and therefore increasing the risk of disease.11-14

Besides to enhance, at least partially, the progression of breast cancer, oxidative stress can also be involved in cancer treatment efficacy.<sup>15</sup> According to previous reports, chemotherapy and/or radiation therapy induced apoptosis by increasing the amount of reactive oxygen species in cancer cells.<sup>15-16</sup> However, excess production of reactive oxygen species can also damage healthy cells, therefore a diet rich in antioxidant may be important to minimize side effects resulted from oxidative damage caused by treatment<sup>15</sup>, in addition to reduce the probability of recurrence.<sup>17</sup>

In addition, cancer treatment may have a direct effect on nutritional status<sup>18</sup>, dietary intake<sup>19</sup> and in the development of food aversion.<sup>19-20</sup>

Therefore, the present study was conducted to investigate the possible changes in dietary intake, anthropometric parameters and oxidative stress markers promoted by breast cancer treatment in women living in the state of Santa Catarina, southern Brazil.

## Subjects and methods

#### Study characterization and design

This is a non-randomized clinical study conducted at the Carmela Dutra Maternity Hospital in Florianópolis City, Santa Catarina, southern Brazil, from October 2006 to June 2008. Clinical, anthropometric, social demographic, dietary intake data and oxidative stress markers were verified in a convenience sample of women with breast cancer in two phases: a) Baseline phase, conducted at the time of breast cancer diagnosis, before cancer treatment (surgery, radiation therapy and/or chemotherapy) and b) Post-treatment phase, after the end of the cancer treatment (considering a maximum period of 20 months).

Women with previous history of cancer and/or benign tumors without suspicion of malignancy, who had already undergone breast surgery, in addition to women who had already started some type of neoadjuvant cancer treatment were excluded from the study. Only women with breast cancer diagnosis confirmed by pathological examinations and living in the state of Santa Catarina were included in the baseline phase the study. Based on these criteria, 55 women were considered eligible to participate in the baseline phase. Out of these, six were excluded from the second phase of the study (post-treatment phase) because they were still under radiation therapy and/or chemotherapy after June 2008. Additionally, nine participants were lost to follow-up in the post-treatment phase for the following reasons: two women refused to return after the end of treatment and seven could not be found after four attempts to contact them by telephone. Therefore, a total of 40 women with breast cancer participated of the study.

All participants signed a free and informed consent form and the research was approved by the Ethics Committee of the Carmela Dutra Maternity Hospital and by the Ethics Committee on Research with Humans of the Federal University of Santa Catarina (protocol number 099/08).

## Clinical data

In order to obtain social demographic and clinical data, a questionnaire adapted from the study conducted by Di Pietro et al.<sup>21</sup> was administered in an interview. The questionnaire contained identification and clinical history information, social demographic and reproductive history questions. Disease's stage was evaluated

from pathological examination results according to the Tumor-Node-Metastasis system.<sup>22</sup> Additionally, information about the type and duration of cancer treatment was collected in the second phase of the study.

## Anthropometric assessment

To measure body weight and height, a mechanical scale with a measuring rod (Filizola Industry S/A, São Paulo, Brazil), with a capacity for 150 kg and 100 g graduation, was used. Anthropometric measurements at the baseline and post-treatment phases were assessed according to the techniques recommended by the World Health Organization. Body weight and height measurements were used to calculate the body mass index (BMI).<sup>23</sup>

### Dietary intake assessment

Habitual dietary intake information was collected in the two study phases by the administration of a food frequency questionnaire (FFQ) adapted from the Sichieri and Everhart validated questionnaire.24 The questionnaire was administered by previously trained nutritionists or undergraduate nutrition students. To help participants identify and report the food intake amounts, were used pictures25 and various sized household utensils (dishes, glasses, cups and spoons). The amounts of food reported as home measures were converted into their respective weights and volumes, in grams (g) or milliliters (mL), respectively, based on the works previously published by Pinheiro et al.26 and Ben.27 Additionally, home measurement conversions (g or mL) of fruit, doughnuts, lard, cream and yerba mate infusion were made by assessing volume and weighing measurements using the technique described by Griswold<sup>28</sup> at the Dietary Technique Laboratory at the Federal University of Santa Catarina. Seasonal foods such as fruits and vegetables had their estimated daily intake calculated considering the season. Dietary intake of all food items obtained by the FFQ use was classified and analyzed for eight food groups described in the Dietary Guide for the Brazilian Population: cereals; tubers and roots; meat and eggs; milk and other dairy products; fruits; beans; vegetables; oils and fats; sugars and sweets.29 The amount of beverages (in mL) with or without alcohol that were not described in the Dietary Guide was also recorded. Additionally, to analyze information about the intake of more specific food, subgroups were created from the eight food groups that make up the Dietary Guide, such as pastry cereals; red meat; fish; poultry; processed meat; fatty meat; low-fat meat; milk and dairy products rich in fat; lean milk and dairy products; fruits rich in vitamin C; fruits rich in carotenoids; cruciferous vegetables; vegetables rich in carotenoids; vegetable fats; and animal fats.

All breast cancer patients did not received any dietary treatment and/or advice during the study; they only got guidance on healthy eating at the time of the interview in the baseline phase.

## Biochemical analysis

For the assessment of oxidative stress markers, blood samples (15 mL) were collected from participants through a puncture of the intermediate arm vein in tubes with or without EDTA to obtain plasma and serum, respectively, by centrifugation (1000 x g/10 min). A whole blood aliquot was used for immediate measurement of blood reduced glutathione (GSH), after red blood cell lyses and protein precipitation with 20% trichloroacetic acid.<sup>30</sup> Measurement of serum antioxidant capacity, thiobarbituric reactive substances in plasma, and serum lipid hydroperoxides levels were made immediately after sample collection, while plasma levels of carbonyls (a marker of plasma protein oxidation) was determined after sample stored at -70 °C for no longer than 30 days.

Serum antioxidant capacity was measured using the ferric reducing antioxidant potential (FRAP) assay, according to the technique proposed by Benzie and Strain.<sup>31</sup> Blood GSH concentration was assessed using the method proposed by Beutler et al.<sup>30</sup> Plasma lipid peroxidation was determined by detecting the substances that react with thiobarbituric acid (TBARS), particularly malondialdehyde, based on the method described by Esterbauer and Cheeseman.<sup>32</sup> The lipid hydroperoxides (LH) present in the serum were quantified by the ferrous oxidation method and complex formation with xylenol orange, as described by Nourooz-Zadeh et al.<sup>33</sup> Carbonyls were measured following the method described by Levine et al.<sup>34</sup> All biochemical tests were made in duplicates.

#### Statistical analysis

Collected data were organized in a double entry database for later statistical analysis with STATA 9.0 software, and in all cases the level of significance was established at 5%.

Continuous data were presented as median, mean and standard deviation and categorical data in the form of absolute and relative frequency.

Normality of data distribution was assessed using the Shapiro-Wilk test. Variables with normal distribution were compared using the paired Student's *t*-test, while the data with non-parametric distribution were compared using the paired Wilcoxon's test.

## Results

Average age of the participants in the beginning of the study was  $51.5 \pm 9.9$  years (range of 35 to 77 years). Most

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#### Table I

Distribution of clinical and therapeutic variables of the women treated for breast cancer (n = 40), Santa Catarina, Brazil

Clinical or therapeutic variable	Number of participants	%
Tumor classification		
Invasive carcinoma	38	95.0
Carcinoma in situ	2	5.0
Tumor stage		
0	2	5.0
Ι	13	32.5
II	17	42.5
III	8	20.0
Axillary lymph node involvement		
Positive	15	37.5
Negative	25	62.5
Surgical procedure		
Radical mastectomy <sup>1</sup>	21	52.5
Partial mastectomy with SLB or axillary		
lymphadenectomy <sup>2</sup>	19	47.5
Radiation Therapy and/or Chemotherapy		
Yes	36	90
Radiation therapy	9	22.5
Chemotherapy	12	30.0
Radiation therapy in association	15	37.5
with Chemotherapy		
No	4	10.0
Hormone therapy		
Yes	32	80
Tamoxifen	27	67.5
Aromatase inhibitor	5	12.5
No	8	20.0
Monoclonal antibody therapy		
Yes	3	7.5
No	37	92.5

<sup>1</sup>Complete removal of breast and axillary lymph nodes. <sup>1</sup>Quadrantectomy or sector resection with sentinel lymph node biopsy (SLB) and/or complete removal of axillary lymph nodes.

women participating in the study were Caucasians (92.5%) and there was a predominance of married women (55.0%). The mean interval of time between the two assessments was  $13.25 \pm 2.92$  months (7 to 20 months).

Clinical and therapeutic characteristics of the 40 women with breast cancer are showed in table I. There

was a prevalence of women with invasive carcinoma (95.0%), stage I or II tumor (75.0%) without involvement of axillary lymph nodes (62.5%). Regarding the type of surgery performed, 52.5% of women underwent radical mastectomy, while 47.5% underwent partial mastectomy with sentinel lymph node biopsy or axillary lymphadenectomy. Out of the 40 participants studied, 32 (80.0%) reported hormone therapy and 27 out of those reported treatment with tamoxifen and five with aromatase inhibitor (anastrozole). In respect to therapies, radiation therapy alone was applied to nine (22.5%) participants, chemotherapy alone was used by twelve (30.0%) women and a combination of both chemotherapy and radiation therapy was used by fifteen (37.5%) women. Four (10%) women did not received either chemotherapy or radiation therapy. Additionally, three (7.5%) patients reported therapy with monoclonal antibodies (trastuzumab).

The anthropometric parameters are shown in table II. A significant increase in the mean body weight (P < 0.005) was found at the end of cancer treatments, which had a direct effect on the mean BMI value (P < 0.005) (table II).

Regarding dietary intake, a significant increase in the intake of the following food groups: meat and eggs (P = 0.02), milk and dairy products (P = 0.01), fruits (P < 0.005), beans (P = 0.04) and oils and fats (P = 0.01), as well as in the following subgroups: read meat (P = 0.03), milk and dairy products rich in fat (P = 0.03), fruits rich in vitamin C (P = 0.01) and vegetable fats (P = 0.02) was observed after treatment (table III). Results for the other food groups and subgroups studied were not statistically significant (data not shown).

Table IV shows the results for biochemical markers of oxidative stress in the baseline and post-treatment phases. There was a significant decrease in the serum antioxidant capacity (P < 0.005) and GSH levels (P < 0.0001), whereas TBARS (P < 0.0001), LH (P < 0.005) and carbonyls (P < 0.0001) levels increased significantly after treatments.

## Discussion

During cancer treatment, agents used in the chemotherapy and radiation therapy can lead to the generation of reactive oxygen species which may dam-

Table II           Anthropometric parameters of women with breast cancer before and after cancer treatments ( $n = 40$ ), Santa Catarina, Brazil					
Anthropometric parameter	Baseline Phase	Post-Treatment Phase	Difference between the Phases	Р	
Weight (kg)	69.40 ± 12.83 (70.7)	71.94 ± 14.17 (70.75)	$2.54 \pm 4.80$ (2.0)	< 0.005 <sup>†</sup>	
BMI <sup>1</sup> (kg/m <sup>2</sup> )	27.68 ± 4.38 (26.95)	28.67 ± 4.65 (28.47)	$0.99 \pm 1.83$ (0.85)	< 0.005 <sup>†</sup>	

BMI: Body Mass Index.

Dara are expressed as mean  $\pm$  standard deviation (median). <sup>†</sup>Paired Student's *t*-test.

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Food groups and subgroups				
(g or mL/day)	Baseline Phase	Post-Treatment Phase	Difference between the Phases	Р
Meat and eggs	145.02 ± 70.05 (145.17)	184.23 ± 101.12 (170.25)	39.21 ± 104.32 (33.17)	0.02*
Red meat	$74.68 \pm 47.76$ (67.38)	105.42 ± 79.53 (98.58)	30.74 ± 81.12 (24.53)	0.03*
Milk and dairy products	314.39 ± 209.95 (387.89)	390.98 ± 256.21 (324.96)	76.59 ± 214.09 (34.74)	$0.01^{\dagger}$
Milk and dairy products rich in fat	197.22 ± 188.19 (131.05)	$276.92 \pm 264.56$ (206.30)	$79.70 \pm 215.78$ (18.63)	0.03 <sup>†</sup>
Fruits	$326.59 \pm 188.77$ (275.48)	503.55 ± 417.45 (398.79)	176.95 ± 370.83 (77.68)	< 0.005
Fruits rich in vitamin C	$212.75 \pm 152.07$ (180.02)	333.00 ± 302.45 (290.29)	120.25 ± 255.34 (57.03)	0.01*
Beans	$65.57 \pm 60.31$ (62.50)	86.37 ± 78.51 (63.56)	$21.00 \pm 84.81$ (6.80)	0.04*
Oils and fats	$30.88 \pm 14.25$ (30.93)	38.93 ± 18.54 (38.42)	$8.05 \pm 17.51$ (3.64)	$0.01^{\dagger}$
Vegetable fat	27.87 ± 14.63 (27.31)	34.97 ± 18.29 (32.65)	7.10±15.82 (4.22)	$0.02^{\dagger}$

Data are expressed as mean ± standard deviation (median). \*Paired Wilcoxon's test; \*Paired Student's *t*-test.

Table IV           Oxidative stress parameters before and after breast cancer treatments ( $n = 40$ ), Santa Catarina, Brazil					
Biochemical parameter	Baseline Phase	Post-Treatment Phase	Difference between the Phases	Р	
Serum AC <sup>1</sup>	658.70±158.35 (677.47)	$550.70 \pm 193.41$ (547.61)	-108 ± 226.80 (-143.52)	< 0.005 <sup>†</sup>	
Whole blood GSH <sup>2</sup>	$1.55 \pm 0.38$ (1.56)	$1.23 \pm 0.41$ (1.20)	-0.32±0.55 (-0.31)	$< 0.0001^{\dagger}$	
Plasma TBARS <sup>3</sup>	$4.95 \pm 0.85$ (4.82)	11.73 ± 6.78 (11.36)	6.78 ± 7.09 (6.33)	< 0.0001*	
Serum LH <sup>4</sup>	$0.90 \pm 0.39$ (0.84)	$1.63 \pm 1.44$ (1.77)	$0.73 \pm 1.44$ (0.88)	< 0.005*	
Plasma protein carbonyl <sup>5</sup>	$0.64 \pm 0.21$ (0.61)	$0.92 \pm 0.13$ (0.88)	$0.28 \pm 0.27$ (0.31)	< 0.0001*	

<sup>1</sup>AC, antioxidant capacity (μmol/L). <sup>2</sup>GSH, reduced glutathione (mmol/L).

<sup>3</sup>TBARS, thiobarbituric acid reactive substances (µmol/L).

<sup>4</sup>LH, lipid hydroperoxides (µmol/L).

<sup>5</sup>(nmol/mg). Data are expressed as mean ± standard deviation (median). \*Paired Wilcoxon's test; \*Paired Student's t-test.

age healthy cells.<sup>15,16</sup> Excess production of reactive oxygen species and the resulting increase in oxidative stress in the body of cancer patients may affect treatment response and contribute to tumor recurrence.35 Therefore, the importance of a diet rich in antioxidant food should be emphasized, not only as a way to protect against disease development and progression, but

also to prevent breast cancer recurrence during and after treatment.15,17

In this study we clearly showed that surgery, chemotherapy and/or radiation therapy increased the levels of oxidative stress biomarkers in women with breast cancer, which could be seen in the significant decrease of antioxidant defense markers (AC and

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GSH) and increased concentrations of lipid (TBARS and LH) and protein (carbonyls) oxidation markers after treatment. Similar results have been reported by other authors who found a reduction in total plasma antioxidant capacity<sup>36</sup> and increased lipid oxidation<sup>36,37</sup> in cancer patients after chemotherapy and/or radiation therapy.

The results of this study have also shown several changes in the dietary intake from the time of disease diagnosis to the end of cancer treatment, particularly an increase in the intake of meats and fats, fruits and beans. The increased consumption of meat and fat by the participants of this study is not in agreement with data previously reported, where breast cancer patients had a significant decrease in the intake of fats<sup>38,39</sup>, meats in general38 and red meat in particular39 after disease diagnosis and/or during cancer treatment. On the other hand, the increased fruit intake by the participants is in agreement with results previously reported by Maskarinec et al.<sup>38</sup>, Salminen et al.<sup>39</sup> and Thomson et al.40 According to evidences in the literature, some women diagnosed with and treated for breast cancer start a healthier diet to improve their health status, prevent disease recurrence or the emergence of new tumors and other related diseases.38,39

A favorable finding in this study was that the increased intake of fruits and beans is in agreement with the recommendations described in the global perspective report on food, nutrition and cancer prevention produced by the World Cancer Research Fund and the American Institute for Cancer Research<sup>41</sup> According to this document, the increased consumption of fruits, non-starchy vegetables, non-processed grains and beans contributes to the prevention of several types of cancer and these recommendations should be also followed by cancer survivors, both during active treatment, when treatment is directed to the tumor in order to prolong patient's survival, and after treatment completion.

The significant increase in the dietary intake of fruit found in this study, particularly fruits rich in vitamin C, can also help the body's defense mechanism against the damage caused by reactive oxygen species, as previously shown in breast cancer survivors. A diet rich in carotenoids, or fruits in general, has decreased oxidative stress and/or improved prognosis in women previously treated for breast cancer.<sup>11,17</sup>

However, the increased intake of meats and fats by the participants of this study is contrary to the recommendations of reports on the global perspective on food, nutrition and cancer prevention.<sup>41</sup> Dietary fat is one of the most investigated nutrients in relation to breast cancer in epidemiological, experimental and clinical studies and several studies have already proven the positive association between high fat intake and carcinogenesis.<sup>12,14</sup> Additionally, it has been suggested that dietary fat can stimulate lipid peroxidation, thus favoring oxidative stress in cancer patients.<sup>12,14</sup> Some studies have also shown that reduced fat intake is associated to lower recurrence rates and longer survival after breast cancer diagnosis.<sup>10</sup> Regarding excess meat intake, particularly red meat, some studies have suggested that these food items represent a risk factor for breast cancer.<sup>21</sup> It should also be mentioned that the intake of red meat by the participants of this study was above the recommended level of 500 g per week. According to the World Cancer Research Fund and the American Institute for Cancer Research, the intake of red meat and processed meat should be limited as a minimum in order to prevent primary and recurrent cancer.<sup>41</sup>

The present study showed a significant increase in the average intake of milk and dairy products rich in fat by the participants during treatment. However, studies that associated the intake of dairy products with disease have shown contradictory results.<sup>42</sup> Regardless, it seems desirable to avoid the intake of dairy products rich in fat, such as whole milk, some types of cheese and cream during and after treatment, since food rich in saturated fat can, generally speaking, favor disease recurrence.<sup>10</sup>

Here, we showed a significant enhancement of weight after treatment, resulting in a mean BMI of 28.67 kg/m<sup>2</sup>, which corresponds to an average increase of 2.54 kg in body weight after cancer treatment. Similar results were found in the studies by Del Rio et al.18 and Ingram and Brown<sup>43</sup>. According to Demark-Wahnefried et al.<sup>44</sup>, weight gain generally ranges from 2.5 to 6.2 kg in the first year after breast cancer diagnosis, particularly in women who undergo chemotherapy as part of their treatment. Although the relationship between excess body weight and the development of breast cancer has not been fully clarified, it should be mentioned that there is evidence showing that weight gain after disease diagnosis can affect survival and recurrence in women with breast cancer.11 Additionally, the average BMI of the participants was not according to the official recommendations of the global perspective report on food, nutrition and cancer prevention in any of the study phases, since the BMI recommendation for breast cancer prevention ranges from 18.5 to 24.9 kg/m<sup>2</sup>, with a median from 21 to 23 kg/m<sup>2</sup>.41

The significant increased in body weight and BMI, as well as the intake of meat and food rich in fat and the increase in oxidative stress markers in these women deserve special attention, since these nutritional and clinical aspects are known risk factors for disease recurrence in addition to the already existing risks linked to treatment procedures performed after disease diagnosis. Based on these data, the importance of nutritional follow-up during and after treatment becomes evident in order to minimize the probability of recurrence or the development of other types of cancer in these survivors. Therefore, advice on a balanced diet rich in antioxidant nutrients that results in weight maintenance may affect positively cancer treatment effectiveness in addition to diminish oxidative and physiological damage caused by cancer treatment.

Finally, some methodological limitations should be considered when interpreting the results of this study. The FFQ used for dietary data collection is considered to be an instrument that estimates previous usual intake in population groups. However, the accurate estimate of usual dietary intake through this instrument is difficult because it relies on the memory of the interviewee to properly estimate intake frequency and the size of food portions.<sup>45</sup>

Although some variation in the estimative of dietary intake needs to be taken into account when evaluating our study, it should be emphasized that care was taken to minimize the potential measurement errors that could result from the instruments of measure, since visual resources were used in order to facilitate the reporting of the dietary intake amounts. Additionally, the FFQ administration, anthropometric assessment and biochemical tests were performed by professionals and nutrition students who were previously trained in data collection methods and instruments. This enhances the reliability of the research and enables the comparison between the assessments of the studied population.

A second limitation refers to the fact the differences in disease stages and the resulting exposure to different treatment protocols did not allow for the identification of the effects of different treatments in relation to biochemical and nutritional results. Additionally, the relationship between changes in dietary intake and changes in oxidative stress in each type of treatment or protocol could not be determined, particularly due to the small sample size. Therefore, new studies should be conducted with larger number of participants in order to confirm these results and get more solid evidence of the effect of different treatment types on dietary intake, anthropometric parameters and oxidative stress in women with breast cancer.

#### Conclusion

The results of this study showed that women undergoing breast cancer treatment, such as surgery, chemotherapy or radiation therapy, increased their intake of meats, fats, dairy products, fruits and beans, had increased body weight and BMI and increased levels of oxidative stress markers.

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## References

- Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Instituto Nacional do Câncer. Coordenação de Prevenção e Vigilância. Estimativa 2010: Incidência de câncer no Brasil. Rio de Janeiro: INCA; 2009.
- Dumitrescu RG, Cotarla I. Understanding breast cancer risk where do we stand in 2005? J Cell Mol Med 2005; 9: 208-21.
- Nkondjock A, Ghadirian P. Risk factors and risk reduction of breast cancer. *Med Sci* 2005; 21: 175-80.
   McPherson K, Steel CM, Dixon JM. Breast cancer-epidemiol-
- MCPherson K, Steel CM, Dixon JM. Breast cancer-epidemiology, risk factors, and genetics. *BMJ* 2000; 321: 624-28.
- Divisi D, Di Tommaso S, Salvemini S, Garramone M, Crisci R. Diet and cancer. Acta Biomed 2006; 77: 118-23.
- Donaldson MS. Nutrition and cancer: a review of the evidence for an anti-cancer diet. *Nutr J* 2004; 3: 19.
- González CA. Nutrition and cancer: the current epidemiological evidence. *Br J Nutr* 2006; 96 (Suppl. 1): S42-5.
- Key TJ, Allen NE, Spencer EA, Travis RC. Nutrition and breast cancer. *Breast* 2003; 12: 412-16.
- Zhang S, Hunter DJ, Forman MR, Rosner BA, Speizer FE, Colditz, GA et al. Dietary carotenoids and vitamins A, C, and E and risk of breast cancer. *J Nat. Cancer Inst* 1999; 91: 547-56.
- Saxe GA, Rock CL, Wicha MS, Schottenfeld D. Diet and risk for breast cancer recurrence and survival. *Breast Cancer Res Treat* 1999; 53: 241-53.
- Rock CL, Demark-Wahnefried W. Nutrition and survival after the diagnosis of breast cancer: a review of the evidence. *J Clin Oncol* 2002; 20: 3302-16.
- Wynder EL, Cohen LA, Muscat JE, Winters B, Dwyer JT, Blackburn G. Breast cancer: weighing the evidence for a promoting role of dietary fat. J Natl Cancer Inst 1997; 89: 766-75.
- Loft S, Poulsen HE. Cancer risk and oxidative DNA damage in man. *J Mol Med* 1996; 74: 297-12.
   Vieira FGV Di Pietro PF Boaventura BCB Ambrosi C Rocken-
- Vieira FGV, Di Pietro PF, Boaventura BCB, Ambrosi C, Rockenbach G, Fausto MA et al. Factors associated with oxidative stress in women with breast cancer. *Nutr Hosp* 2011; 26: 528-36.
- 15. Borek C. Dietary antioxidants and human cancer. *Integr Cancer Ther* 2004; 3: 333-41.
- Borek C. Antioxidants and radiation therapy. J Nutr 2004; 134: 3207S-09S.
- Thomson CA, Stendell-Hollis NR, Rock CL, Cussler EC, Flatt SW, Pierce JP. Plasma and dietary carotenoids are associated with reduced oxidative stress in women previously treated for breast cancer. *Cancer Epidemiol Biomarkers Prev* 2007; 16: 2008-15.
- Del Rio G, Zironi S, Valeriani L, Menozzi R, Bondi M, Bertolini M, et al. Weight gain in women with breast cancer treated with adjuvant cyclophosphomide, methotrexate and 5-fluorouracil. Analysis of resting energy expenditure and body composition. *Breast Cancer Res Treat* 2002; 73: 267-73.
- Lancheros L, Gamba M, González H, Sánchez R. Caracterización de la evolución del estado nutricional de pacientes con cáncer de mama en tratamiento quimioterapéutico. *Rev Colomb Cancerol* 2004; 8: 11-22.
- Arnes HG, Gee MI, Hawrysh ZJ. Taste perception and breast cancer: evidence of a role for diet. J Am Diet Assoc 1993; 93: 541-46.
- Di Pietro PF, Medeiros NI, Vieira FG, Fausto MA, Bello-Klein A. Breast cancer in southern Brazil: association with past dietary intake. *Nutr Hosp* 2007; 22: 565-72.
- Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Instituto Nacional de Câncer. TNM: classificação de tumores malignos. 6. ed. Rio de Janeiro: INCA; 2004.
- World Health Organization. Phisical Status: the use and interpretation of anthropometry, WHO technical report, series 854. Geneva: WHO; 1995.
- Sichieri R, Everhart MD. Validity of a brazilian frequency questionnaire against dietary recalls and estimated energy intake. *Nutr Res* 1998; 19: 1649-59.
- Zabotto CB. Registro fotográfico para inquéritos dietéticos. Campinas: Unicamp; 1996.
- Pinheiro ABV, Lacerda EMA, Benzecry EH, Gomes MCS, Costa VM. Tabela para avaliação de consumo alimentar em medidas caseiras. 2<sup>th</sup> ed. São Paulo: Atheneu; 2004.

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- Ben ML. Quanto pesa?: tabela de pesos e medidas de alimentos. Porto Alegre: Ediplat; 2007.
- Griswold RM. Estudo Experimental dos Alimentos. São Paulo: Edgard Blücher; 1972.
- 29. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Coordenação-Geral da Política de Alimentação e Nutrição. Guia Alimentar para a população brasileira: promovendo a alimentação saudável. Brasília: Ministério da Saúde; 2006.
- Beutler E, Duron O, Kelly BM. Improved method for the determination of blood glutathione. J Lab Clin Med 1963; 61: 882-90.
- Benzie IFF, Strain JJ. The ferric reducing ability of plasma (frap) as a measure of antioxidant power: the frap assay. *Anal Biochem* 1996; 239: 70-76.
- Esterbauer H, Cheeseman K. Determination of aldehydic lipid peroxidation products: malonaldehyde and 4-hydroxynonenal. *Methods Enzymol* 1990; 186: 407-21.
- Nourooz-Zadeh J, Tajaddini-Sarmadi J, Wolff SP. Measurement of plasma hydroperoxide concentrations by the ferrous oxidation-xylenol orange assay in conjunction with triphenylphosphine. *Anal Biochem* 1994; 220: 403-09.
- Levine RL, Garland D, Oliver CN, Amici A, Climent I, Lenz AG et al. Determination of carbonyl content in oxidatively modified proteins. *Methods Enzymol* 1990; 186: 464-78.
- Conklin KA. Chemotherapy-associated oxidative stress: impact on hemotherapeutic effectiveness. *Integr Cancer Ther* 2004; 3: 294-300.
- Durken M, Herrnring C, Finckh B, Nagel S, Nielsen P, Fischer R et al. Impaired plasma antioxidative defense and increased nontransferrin-bound iron during high-dose chemotherapy and

radiochemotherapy preceding bone marrow transplantation. *Free Radi. Biol Med* 2000; 28: 887-94.

- Cetin T, Arpaci F, Yilmaz MI, Saglam K, Ozturk B, Komurcu S et al. Oxidative stress in patients undergoing high-dose chemotherapy plus peripheral blood stem cell transplantation. *Biol Trace Elem Res* 2004; 97: 237-47.
- Maskarinec G, Murphy S, Shumay DM, Kakai H. Dietary changes among cancer survivors. *Eur J Cancer Care* 2001; 10: 12-20.
- Salminen E, Heikkila S, Poussa T, Lagstrom H, Saario R, Salminen S. Female patients tend to alter their diet following the diagnosis of rheumatoid arthritis and breast cancer. *Prev Med* 2002; 34: 529-35.
- Thomson CA, Flatt SW, Rock CL, Ritenbaugh C, Newman V, Pierce JP. Increased fruit, vegetable and fiber intake and lower fat intake reported among women previously treated for invasive breast cancer. J Am Diet Assoc 2002; 102: 801-08.
- World Cancer Research Fund; American Institute For Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington, DC: AICR; 2007.
- of cancer: a global perspective. Washington, DC: AICR; 2007.
  42. Moorman PG, Terry PD. Consumption of dairy products and the risk of breast cancer: a review of the literature. *Am J Clin Nutr* 2004; 80: 5-14.
- Ingram C, Brown JK. Patterns of weight and body composition change in premenopausal women with early stage breast cancer: has weight gain been overestimated? *Cancer Nurs* 2004; 27: 483-90.
- Demark-Wahnefried W, Rimer BK, Winer EP. Weight gain in women diagnosed with breast cancer. J Am Diet Assoc 1997; 97: 519-29.
- Willet WC. Nutritional Epidemiology. New York: Oxford University; 1998.