

Original/Síndrome metabólico

# Nutritional and metabolic status of breast cancer women

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## Abstract

**Introduction:** The nutritional and metabolic status have been related to cancer risk factors as well as to cancer treatment morbimortality. Thus, its assessment is important for developing strategies for the promotion, maintenance and / or recovery of nutritional status and cancer outcome.

**Material and methods:** Several different methods for nutritional assessment in breast cancer patients undergoing adjuvant therapy were used, including subjective global assessment (SGA), body mass index (BMI), triceps skinfold (TSF), mid-arm circumference (MAC), adductor pollicis muscle thickness (APMT), hand grip strength (HGS) and bioelectrical impedance analysis (BIA). The presence of metabolic syndrome (MetS) was also evaluated. The occurrence of complications during cancer treatment versus the nutritional status was assessed.

**Results:** We followed 78 women with a mean age of  $53.2 \pm 11.6$  years. Most patients were considered well nourished (80.8%). Excessive body fat mass by BIA and MetS were found in 80,8 % and 41.9% of the patients respectively. There were significant differences in BMI, TSF, WC (waist circumference) and % fat mass between patients with and without MetS. Most patients experienced complications during cancer treatment, but there was no association with nutritional or metabolic status.

**Conclusion:** In breast cancer women undergoing adjuvant therapy, the prevalence of metabolic syndrome was high and, on the contrary, undernutrition was low. There were no short-term effects of metabolic syndrome or undernutrition on clinical outcomes.

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Keywords: Breast cancer. Nutritional status. Metabolic syndrome.

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## EL ESTADO NUTRICIONAL Y METABÓLICO DE LAS MUJERES CON CÁNCER DE MAMA

### Resumen

**Introducción:** El estado nutricional y metabólico se han relacionado con factores de riesgo del cáncer, así como la morbimortalidad del tratamiento del cáncer. Por lo tanto, su evaluación es importante para el desarrollo de estrategias para la promoción, mantenimiento y/o recuperación del estado nutricional y la evolución del cáncer.

**Material y métodos:** Se utilizaron varios métodos diferentes para la evaluación nutricional en pacientes con cáncer de mama sometidas a terapia adyuvante, incluyendo la valoración subjetiva global (SGA), el índice de masa corporal (IMC), pliegue tricipital (PT), la circunferencia del brazo (CB), del espesor del músculo aductor del pulgar (TAPM), la fuerza de presión manual (FPM) y el porcentaje de masa grasa (PMG) mediante impedancia bioeléctrica. También se evaluó la presencia del síndrome metabólico (SM). Se evaluó la aparición de complicaciones durante el tratamiento del cáncer en comparación con el estado nutricional.

**Resultados:** Se siguieron a 78 mujeres con una edad media de  $53,2 \pm 11,6$  años. La mayoría de los pacientes estaban bien nutridos (80,8 %). Excesiva PMG y los SM se encontraron en 80,8 % y 41,9 % de los pacientes, respectivamente. Hubo diferencias significativas en el IMC, PT, circunferencia de la cintura y la PMG entre los pacientes con y sin síndrome metabólico. La mayoría de los pacientes experimentaron complicaciones durante el tratamiento del cáncer, pero no hubo asociación con el estado nutricional o metabólico.

**Conclusión:** En las mujeres con cáncer de mama que reciben terapia adyuvante, la prevalencia del síndrome metabólico fue alta y, por el contrario, la desnutrición era baja. No hubo efectos a corto plazo del síndrome metabólico o la desnutrición en los resultados clínicos.

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Palabras clave: Cáncer de mama. Estado nutricional. Síndrome metabólico.

## Abbreviations

APMT: Adductor pollicis muscle thickness.  
BIA: Bioelectrical impedance analysis.  
BMI: Body mass index.  
FFM: Fat-free mass.  
FM: Fat mass.  
GLIC: Fasting glucose.  
HC / UFMG: Hospital das Clinicas, Universidade Federal de Minas Gerais.  
HDL: High-density lipoprotein cholesterol.  
HGS: Hand grip strength.  
LDL: Low-density lipoprotein cholesterol.  
MAC: Mid-arm circumference.  
MetS: Metabolic syndrome.  
SGA: Subjective global assessment.  
SPSS: Statistical Package for Social Sciences.  
TG: Hypertriglyceridemia.  
TSF: Triceps skinfold.  
VLDL: High very low-density lipoprotein cholesterol.  
WC: Waist circumference.

## Introduction

Breast cancer is the most common type of tumor and the leading cause of cancer death in women. It accounts for 23% (1,380,000) of all new cancer cases and 14% (458,400) of all cancer deaths<sup>1</sup>. The nutritional status plays a key role both on the risk factors for breast cancer<sup>2-4</sup> as well as on the anticancer treatment outcome<sup>5,6,7</sup>.

Obesity is a risk factor for the development of breast cancer in women after menopause. The adipose tissue should be observed as a metabolically active endocrine tissue that causes an increase in circulating sex hormones, insulin resistance and the increased production of proinflammatory cytokines<sup>8</sup>. These metabolic changes also lead to the development of metabolic syndrome (MetS)<sup>9</sup>, which is a complex disorder consisting of a set of cardiovascular risk factors and increased risk of breast cancer recurrence<sup>10</sup>. The main components of MetS are hypertension, insulin resistance, obesity and dyslipidemia<sup>11</sup>. The increase in the incidence of breast cancer in recent decades has been accompanied by an increase in the frequency of MetS<sup>12</sup>. On the other hand, it is important to note that the prevalence of undernutrition in cancer patients ranges from 40% to 80%<sup>13</sup>. The IBRANUTRI, a multicenter, cross-sectional, epidemiologic study on hospital undernutrition, showed that cancer patients had an almost three-fold higher undernutrition rate than non-cancer patients<sup>14</sup>. Undernutrition is associated with increased morbidity, mortality, longer hospital stays and higher medical costs<sup>15</sup>. Furthermore, in cancer patients, undernutrition is associated with low treatment efficacy<sup>16</sup>.

The accuracy of nutritional diagnosis, as currently there is no gold standard technique, maybe overcome by the combination of several nutritional and metabolic

indicator, which can improve the precision of the diagnosis<sup>17</sup>. The subjective global assessment (SGA) proposed by Detsky et al.<sup>18</sup> is essentially a clinical method for the assessment of nutritional status. Anthropometric indicators, such as body mass index (BMI), triceps skinfold (TSF), and mid-arm circumference (MAC) are inexpensive and easy to apply, and they provide immediate results, but they usually reflect body composition rather than nutritional status<sup>19</sup>. The adductor pollicis muscle thickness (APMT) is a relatively new anthropometric parameter that has been used to assess the muscle compartment and, indirectly, nutritional status<sup>20</sup>. Bioelectrical impedance analysis (BIA) has also been used to assess body composition in patients with cancer. Hand grip strength (HGS), a functional test of skeletal muscle, has received increased attention from clinicians and researchers in recent years because skeletal muscle function is impaired and muscle strength decreases in the presence of malnutrition<sup>21</sup>.

Therefore, the aim of the present study was to evaluate the nutritional and metabolic status of patients with breast cancer and its association with complications in cancer treatment.

## Materials and methods

The present study was a prospective and descriptive study performed in Hospital Borges da Costa/Hospital das Clínicas/Universidade Federal de Minas Gerais, Brazil. Patients over 18 years old who were diagnosed with breast cancer and before they were started on chemo or radiotherapy were invited to participate in the study. Patients with infectious disease, non-cancer inflammatory diseases, or kidney and liver diseases were excluded. All patients provided informed consent.

A standardized questionnaire was used to collect data, including name, age, sex, menopausal status and age of menarche. The nutritional status assessment was carried out using various methods. Anthropometric measurements, including BMI, TSF, MAC and APMT were performed by trained dietitians. The body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters, and the nutritional status of adult patients was determined according to the World Health Organization criteria<sup>22</sup>. Elderly individuals were classified according to the Pan American Health classification<sup>23</sup>. Both MAC and TSF were classified as described by Frisancho, 1990<sup>24</sup>. The APMT was classified according to the values proposed by Gonzalez et al.<sup>25</sup>, using the highest value of three measurements. Body composition (fat mass and fat-free mass) was measured by bioimpedance, and the percent body fat was calculated as described by Lohman et al.<sup>26</sup>. HGS was performed with the patient in the sitting position with the arms on a table and the average of three measurements was used<sup>27</sup>. Subjective Global Assessment (SGA) was used as the gold standard to assess the nutritional status, and patients were

classified as well nourished, suspected or moderately malnourished and severely malnourished<sup>18</sup>.

Metabolic syndrome was diagnosed according to the criteria published by the International Diabetes Federation<sup>11</sup>.

The cancer stage was obtained from the medical records as well as data on complications. The latter were classified using the Common Toxicity Criteria, version 3<sup>28</sup> as follows: hematologic toxicity (leucopenia and thrombocytopenia); gastrointestinal toxicity (nausea, vomiting, diarrhea and mucositis); fever and asthenia. Complications were evaluated for a period of three months after initiation of treatment. Data were collected before the initiation of chemotherapy or radiotherapy treatment.

This research has been conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki. The research was reviewed and approved by the Ethics Committee (ETIC 0601.0.203.000-0). Statistical Package for Social Sciences (SPSS) version 19.0 software was used for statistical analyses. A p value <0.05 was considered statistically significant. Spearman and Pearson correlation coefficients were used to verify the correlation between anthropometric measures of adiposity and biochemical tests. The chi-square test was used to assess the associations between MetS and tumor stage and between MetS and menopausal status. The associations between MetS and complications were assessed by Fisher's exact test. Student's t-test was used to compare nutritional assessment parameters with the presence and absence of MetS.

## Results

A total of 78 women with a mean age of 53.2 ± 11.6 years, (31-79 years) were evaluated. The general population data are shown in table I. Of this group, 59% (n = 46) were postmenopausal, and of these, 26.1% (n = 12) were undergoing hormone replacement therapy. Menarche prior to twelve years old was reported by 35.9% (n = 28) of the patients, and late menopause was observed in 35.9% of the patients. Advanced stage (III/IV) tumors were diagnosed in 48.7% of the patients.

The nutritional status of the patients as determined using different methods is shown in table II. Most of the patients were considered well nourished, independently of the method used. Excess weight (overweight or obesity) was found in 57.7% using BMI and in 16.7%, 33.3%, 80.8% and 88.5% using MAC, TSF, WC and % FM measured by BIA, respectively. Despite this, 19.2% (n = 15) patients were classified as suspected or moderately malnourished by SGA. However, according to the APMT, PA and HGS, all patients were considered within the normal range.

Biochemical parameter analyses showed that 51.6% of the patients exhibited high cholesterol; 12.9% had increased low-density lipoprotein cholesterol (LDL);

**Table I**  
General characteristics of patients with breast cancer (n= 78)

Characteristics	N (%)
<b>Age</b>	
30- 40	10 (12.8)
41-59	49 (62.8)
≥ 60	19 (24.4)
<b>Associated diseases</b>	51 (65.4)
<b>Early menarche (≤ 12 years)</b>	28 (35.9)
<b>Menopausal status</b>	
Premenopausal	32 (41.0)
Postmenopausal	46 (59.0)
<b>Late menopause (≥ 55 years)</b>	28 (35.9)
<b>Hormone replacement therapy</b>	12 (26.1)
<b>Tumor Stage</b>	
I / II	40 (51.3)
III / IV	38 (48.7)

**Table II**  
Distribution of patients with breast cancer according to nutritional status parameters (n= 78)

Variables	N (%)
<b>Subjective global assessment (SGA)</b>	
Severe malnourished	0 (0)
Suspected or moderately malnourished	15 (19.2)
Well nourished	63 (80.8)
<b>Body mass index (BMI)</b>	
Low weight	3 (3.8)
Eutrophic	30 (38.5)
Overweight	19 (24.4)
Obese	26 (33.3)
<b>Triceps skinfold thickness (TSF)</b>	
Malnourished (percentile < 15)	5 (6.4)
Eutrophic (percentile 15-85)	47 (60.3)
Obese (percentile > 85)	26 (33.3)
<b>Waist circumference (WC)</b>	
Normal (< 80 cm)	9 (11.5)
Increased (≥ 80 cm)	69 (88.5)
<b>Mid-arm circumference (MAC)</b>	
Malnourished (percentile < 15)	9 (11.5)
Eutrophic (percentile 15-85)	56 (71.8)
Obese (percentile > 85)	13 (16.7)
<b>Adductor pollicis muscle (APM)</b>	
Malnourished (≤ percentile 5)	8 (10.3)
Eutrophic (> percentile 5)	70 (89.7)
<b>% Fat mass (FM)</b>	
Malnourished (≤ 22%)	2 (2.6)
Eutrophic (22.1% – 31.9%)	13 (16.6)
Obese (≥ 32%)	63 (80.8)
<b>Phase angle (PA)</b>	
Malnourished (< percentile 5)	10 (12.8)
Eutrophic (≥ percentile 5)	68 (87.2)
<b>Handgrip strength (HGS)</b>	
Malnourished (≤ percentile 5)	7 (9.0)
Eutrophic (> percentile 5)	71 (91.0)

**Table III**  
Distribution of patients with breast cancer according to biochemical parameters (n= 78)

Variable	N (%)
<b>Total cholesterol (TC)</b>	
Normal (< 200 mg/dL)	30 (48.4)
High (≥ 200 mg/dL)	32 (51.6)
<b>High-density lipoprotein cholesterol (HDL)</b>	
Normal (≥ 50mg/dl)	37 (59.7)
Low (< 50mg/dl)	25 (40.3)
<b>Low-density lipoprotein cholesterol (LDL)</b>	
Normal (<160 mg/dL)	54 (87.1)
High (≥ 160 mg/dL)	8 (12.9)
<b>Very low-density lipoprotein cholesterol (VLDL)</b>	
Normal (< 30 mg/dL)	48 (77.4)
High (≥ 30 mg/dL)	14 (22.6)
<b>Triglycerides (TG)</b>	
Normal (< 150 (mg/dL)	49 (79.0)
High (≥ 150 (mg/dL)	13 (21.0)
<b>Glycemia (GLIC)</b>	
Normal (<100 mg/dL)	43 (69.4)
High (≥ 100 mg/dL)	19 (30.6)

22.6% had high very low-density lipoprotein cholesterol (VLDL), 40.3% had low high-density lipoprotein cholesterol (HDL) and 21% had hypertriglyceridemia (TG). Elevated fasting glucose (GLIC) values were found in 30.6% of patients (Table III).

Weight, BMI, WC, MAC and %FM correlated negatively with HDL and positively with VLDL, TG and fasting glucose (p <0.05). In contrast, the % FFM was positively correlated with HDL and negatively correlated with VLDL, TG and fasting glucose (p < 0.05). Total cholesterol and LDL were not significantly co-

related with any analyzed variable. Other correlations are described in table IV.

We were able to assess 62 patients for the presence of MetS; data for the remaining patients were incomplete, these were not show in medical records or were not requested by doctors. MetS was diagnosed in 41.9% (n = 26) of the patients. Of these, 23.1% (n = 6) were classified as eutrophic, 15.4% (n = 4) were overweight and 61.5% (n = 16) were classified as obese by BMI. Excess body fat, as measured by BIA, was found in 92.3% (n = 24) of patients in the MetS group.

Tumor stage was not associated with MetS (p=0.46) (Fig. 1). There was a significant association between menopausal status and MetS (p= 0.01); Postmenopausal women presented with 69.2% of MetS (Fig. 2).

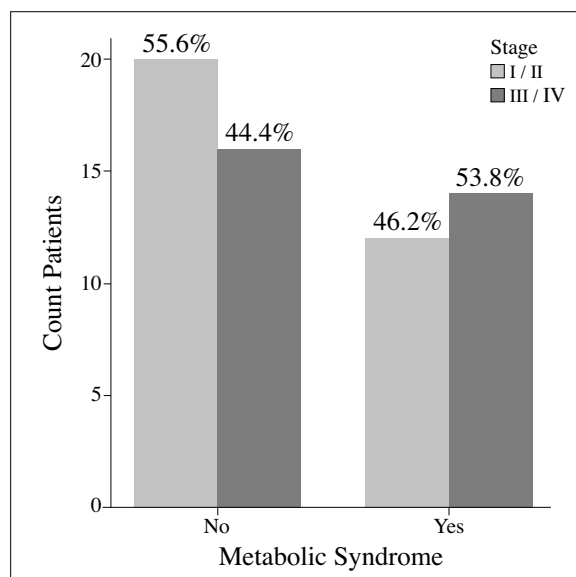


Fig. 1.—Prevalence of metabolic syndrome in women with breast cancer according to tumor stage (p > 0.05).

**Table IV**  
Correlation of anthropometric measurements and body composition with biochemical parameters in patients with breast cancer (n= 78)

Variables	Biochemical parameters					
	CT <sup>1</sup> r	HDL <sup>1</sup> r	LDL <sup>1</sup> r	VLDL <sup>1</sup> r	TG <sup>2</sup> r	GLIC <sup>2</sup> r
Weight (kg)	0.03	-0.36*	0.04	0.36*	0.33*	0.32*
BMI (kg/m <sup>2</sup> )	0.05	-0.36*	0.03	0.46*	0.40*	0.40*
TSF (mm)	0.03	-0.40*	0.09	0.25	0.30*	0.28*
WC (cm)	0.02	-0.38*	0.01	0.45*	0.40*	0.40*
MAC (cm)	0.02	-0.43*	0.04	0.38*	0.40*	0.35*
FM (%)	0.04	-0.35*	0.05	0.37*	0.33*	0.30*
FFM (%)	0.09	0.31*	-0.009	-0.28*	-0.27*	-0.28*

BMI = body mass index; TSF = triceps skinfold; WC = waist circumference; MAC = mid-arm circumference; FM = fat mass; FFM = fat-free mass; \*p<0.05; <sup>1</sup>Pearson correlation; <sup>2</sup>Spearman correlation.

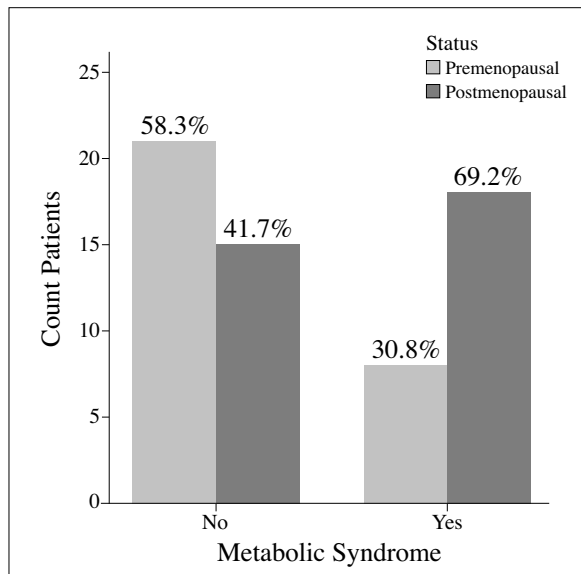


Fig. 2.—Prevalence of metabolic syndrome in women with breast cancer according to menopausal status ( $p = 0.01$ ).

A comparison of the data for MetS and anthropometric indicators (BMI, TSF, MAC, and APMT), body composition (% FM and % FFM), PA and HGS is shown in Table V. There were significant differences in BMI, TSF, WC, % FM and % FFM between patients with and without MetS.

Complications from treatment were evaluated in only 69 patients, as data were missing from the remaining records as well as data from patients undergoing treatment with hormone therapy since they discontinued their follow up at the outpatient clinic. Of these, 85.5% ( $n = 59$ ) presented with complications. Figure 3 depicts the frequency of complications during a follow-up period of three months of antineoplastic treat-

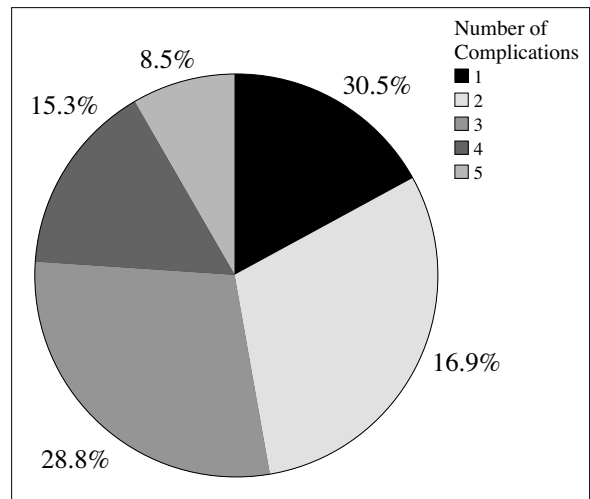


Fig. 3.—Number of complications during anticancer treatment in patients with breast cancer.

ment. Most patients had two to three complications. Figure 4 shows the types of complications presented during anticancer treatment. There was no association between nutritional and metabolic status and the presence of complications ( $p = 0.59$ ).

## Discussion

A high prevalence of overweight and obesity was observed in breast cancer women while undernutrition was low, yet present among these women. Although we were not able to show any association between nutritional and metabolic status and outcome, which was certainly due to the short term follow up of these patients, this aspect is of particular concern among breast

**Table V**  
Comparison of anthropometric and body composition measurements between the groups with and without MetS ( $n = 78$ )

Variables	No metabolic syndrome ( $n = 36$ )		With metabolic syndrome ( $n = 28$ )		P- value
	Mean	SD	Mean	SD	
BMI(kg/m <sup>2</sup> )	25.3	± 4.3	30.9	± 5.5	<b>&lt;0.001</b>
TSF (mm)	29.2	± 11.7	37.5	± 12.0	<b>0.006</b>
MAC (cm)	30.0	± 4.5	33.7	± 3.8	<b>0.04</b>
WC (cm)	88.2	± 10.1	101.3	± 12.1	<b>&lt;0.001</b>
APMT (mm)	20.9	± 4.3	22.5	± 4.1	0.14
FM (%)	35.4	± 6.5	42.2	± 6.2	<b>&lt;0.001</b>
FFM (%)	63.8	± 7.9	57.7	± 6.2	<b>0.002</b>
PA	5.8	± 1.0	5.7	± 0.8	0.62
HSG (kg)	21.7	± 4.7	21.1	± 5.9	0.63

BMI = body mass index; TSF = triceps skinfold; MAC = mid-arm circumference; WC = waist circumference; APMT = adductor pollicis muscle thickness; FM = fat mass; FFM = fat-free mass; PA = phase angle; HSG = hand grip strength. Student's t test

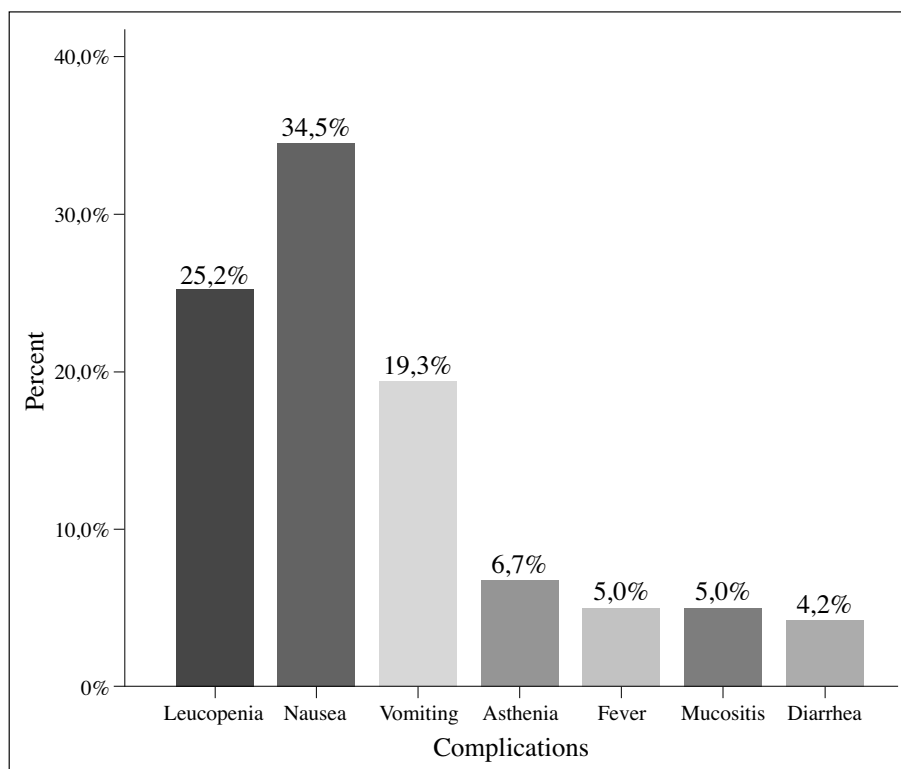


Fig. 4.—Complications developed during anticancer treatment in patients with breast cancer.

cancer patients. A prospective study conducted in Denmark including women diagnosed with breast cancer showed that patients with a BMI of 30 kg/m<sup>2</sup> or higher had more advanced disease at diagnosis compared with patients with a BMI below 25 kg/m<sup>2</sup>. When the data were adjusted for disease characteristics, patients with a BMI of 30 kg/m<sup>2</sup> or more exhibited a significant increase in the risk of developing distant metastases after 10 years (increased by 46%) and in the risk of dying as a result of breast cancer after 30 years (increased by 38%). Also, both chemotherapy and endocrine therapy seemed to be less effective after 10 or more years for patients with BMI greater than 30 kg/m<sup>2</sup>.

Therefore, it is of utmost importance that the nutritional status of breast cancer women is routinely assessed and, easy anthropometric measures such as BMI and waist circumference should be performed as part of the treatment of these patients.

On the other hand, the high rate of increased BMI among women with breast cancer may hamper the identification of nutritional status deficiency. Because nutrition status assessment is commonly neglected, this may be a particular problem among these women, as undernutrition is associated with poorer outcome and prognosis, decreased quality of life and worse functional status<sup>29, 30, 31</sup>. In the current study, 19.2% of the patients were classified as suspected or moderately malnourished when assessed by SGA, an essential clinical assessment instrument. Dahlk et al.<sup>32</sup> found that 29.1% of patients with breast cancer exhibited undernutrition. SGA allows the early identification of patients with

deficient nutritional status, especially in patients with altered body composition markers due to overweight and obesity<sup>33, 34</sup>. Thus, the presence of undernutrition should be investigated in patients with breast cancer, even those with excess body fat and, since there are several tools, which present high intervariability diagnosis, it is suggested that a clinical method be used.

We also observed a high prevalence of MetS (41.9% of patients). Contrary to our data, Capasso et al.<sup>35</sup> found a lower prevalence of MetS (30%) in patients with breast cancer. However, in the current study, the majority of women with MetS were postmenopausal, as found in the study by Cho et al.<sup>36</sup> We did not observe any association between disease stage and MetS, which was reported by Healy et al., 2010, who showed that patients with more advanced stages of the disease had greater central obesity and higher rates of hyperglycemia and hyperinsulinemia<sup>4</sup>.

We observed higher values of body composition parameters such as BMI, TSF, MAC, WC, %FM and lower values of % FFM ( $p < 0.05$ ) among MetS patients and this is of utmost importance as the latter is a prognostic factor for breast cancer recurrence<sup>10</sup>.

The present study demonstrated the importance of emphasizing the role of nutritional assessment by different methods and also the use of biochemical parameters to evaluate nutritional and metabolic impairment as well as MetS. The use of any one of these parameters in isolation produces questionable results due to the errors inherent in each of these methods. Thus, the combination of several indicators may im-

prove the precision and accuracy of nutritional diagnosis<sup>19</sup> which is fundamental in cancer patients.

## Conclusions

In conclusion, while the prevalence of excess body fat and metabolic syndrome were high, undernutrition was low, although the latter was also seen among obese women. There were no short-term effects of nutritional and metabolic status on clinical outcome in this study. However, we recommend that the nutritional and metabolic status be routinely assessed among these patients due to the high prevalence of nutritional and metabolic imbalances, which are reported relevant impact factors on cancer patient outcomes.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

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