



## Assessment of the nutritional and metabolic profile of women with breast cancer and its association with metabolic syndrome

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### 1. Introduction

Cancer is a relevant public health problem because of its increased incidence, morbidity and mortality. According to the World Health Organization (WHO), approximately 80% of the 20 million new cases expected for 2015 would occur in developing countries [1].

Among the various types of neoplasia, breast cancer is the one that most affects women every year, being responsible for 23% (1380,000) of all new cases of cancer and 14% (458,400) of all deaths due to cancer [2,3], with 57,950 new cases being projected for 2016/2017 in Brazil [4]. The nutritional status and dietary intake of the patient plays a key role both regarding the risk factors for breast cancer [5,6] and the results of its treatment [7].

Obesity is a risk factor for the development of breast cancer in women, especially after menopause and has an adverse prognostic effect on the survival of these women. Adipose tissue should be considered to be a metabolically active endocrine tissue and excess body fat appears to influence the development and progression of breast cancer due to increased estrogen synthesis, insulin resistance and activation of inflammatory pathways [8,9]. Studies have suggested associations between body fat, body mass index (BMI) and waist circumference (WC) as risk factors for the development of breast cancer [4,10]. In addition, the stress caused by the

diagnosis and chemotherapeutic treatment of breast cancer has been related to weight gain due to changes in life style characterized by physical inactivity and inappropriate eating habits [11,12].

These metabolic changes also lead to the development of metabolic syndrome (MS) [13], a complex disorder consisting of a set of cardiovascular risk factors and an increased risk of breast cancer recurrence [14]. The main components of MS are systemic arterial hypertension (SAH), insulin resistance, obesity and dyslipidemia [15] and several studies have demonstrated that the increased incidence of breast cancer over the last decades has been accompanied by an increased frequency of MS [16,17].

In Brazil, studies show high prevalence rates of MS in the population. One of these population-based studies, with adults, found a prevalence of 29.8% (CI95% 28–32) of SM [18]. Another study, carried out with elderly found that the overall prevalence of MS was 58.6% (95% CI 49.8–67.1), and for men this percentage was (95% CI: 41.3–69.5) and for women 60.5% (CI95% 49.1–71.2) [19].

In view of this, it is possible to observe that the prevalence of MS in women with breast cancer follow this tendency. A study carried out with this public shows that MS was present in 50% of the surviving women, when compared with the control group that found 37.5% of participants with MS. In this study, the most frequent diagnostic criteria were: abdominal obesity (62.5%) and dyslipidemia (45.2%) [20]. Another study, also carried out with women with breast cancer, found that 69.2% of postmenopausal women had MS and 53.8% had advanced stages of cancer, demonstrating that MS could influence the worsening of cancer prognoses of breast [4].

Thus, knowledge about the nutritional and metabolic profile of breast cancer patients represents an important measure for the development of multiprofessional actions aiming at the elaboration of strategies directed at the various phases of the disease and its treatment [21].

Early detection of MS in women during breast cancer treatment is very important, since such comorbidity raises cardiovascular risk, is related to prior prognosis of cancer, increases the risk of death and causes a negative impact on the quality of life of women [22].

On this basis, considering the lack of studies in the literature evaluating the possible association of breast cancer with the metabolic syndrome in Brazil, and none of them compare different

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diagnostic criteria, this present study aimed to assess the nutritional and metabolic profile of women with breast cancer and its possible association with MS according to the criteria of the WHO [23], of the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) [24] and of the International Diabetes Federation (IDF) [25]. The study was conducted on women with breast cancer seen at a rehabilitation nucleus located in the interior of the state of São Paulo.

## 2. Methods

### 2.1. Subjects

This was an observational, descriptive cross-sectional study conducted from September to November 2015 at a rehabilitation nucleus for women with breast cancer called Nucleus of Teaching, Research and Assistance in the Rehabilitation of Mastectomizados located in the School of Nursing of Ribeirão Preto (EERP) of the University of São Paulo (USP), in the city Ribeirão Preto, São Paulo, Brazil. This rehabilitation center offers comprehensive assistance to women affected by breast cancer, offering biopsychosocial support through a multiprofessional team consisting of nurses, physiotherapists, nutritionists and psychologists. The study was approved by the Research Ethics Committee of the institution (protocol no. CAEE: 41688915.3.0000.5393) and all subjects gave written informed consent to participate.

All women who participated in the activities of the rehabilitation nucleus from January to December 2014 ( $n = 224$ ) were considered for the study sample. Of these, 15 died and 65 were excluded because they did not satisfy the inclusion criteria of the study. Of the 144 women left, 77 were excluded for refusal to participate or for the impossibility of contact, with a final sample of 67 participants being left.

Inclusion criteria were: age of more than 18 years and being a participant in the rehabilitation nucleus who had been diagnosed and treated at the University Hospital, Faculty of Medicine of Ribeirão Preto, University of São Paulo. Exclusion criteria were: advanced metastatic disease or absence of clinical conditions for participation; amputated or immobilized limbs; generalized edema and/or ascites, and presence of heart pacemaker, aneurysm clip or metal implants of any type (metal wires, plates or screws).

The anthropometric measurements obtained were weight, height, waist, hip, arm and calf circumference, and skin folds. Handgrip strength was also measured. All measurements were made in triplicate and the mean of the three values was used, except for handgrip strength. Weight was measured with a Welmy electromechanical digital scale for adults with a maximum capacity of 200 kg and 100 g divisions, calibrated by a qualified company before data collection. Height was measured with an anthropometric ruler coupled to the scale with 0.5 cm precision and with a maximum extension of 2 m. BMI was calculated as weight in kg divided by height squared in meters and the nutritional status of the patients was determined according to the criteria of the WHO [26] for adult patients and according to the criteria of the Pan-American Health Organization for elderly women [27]. The waist/hip ratio (WHR) was calculated and the value of 0.85 was used to determine cardiovascular risk [26].

The waist, hip, arm and calf circumferences were measured as recommended by Lohman et al. (1988) [23]. Tricipital, bicipital, subscapular and suprailliac skin folds were measured on the right body half of the patients and percent body fat (% BF) was estimated using the values adopted by Durmin and Womersley [28] and classified according to the values proposed by Lohman et al. (1992) [29]. The handgrip strength test was carried out using a Handgrip digital dynamometer mode ChardeMG4800. A standardized

position was used, with the subject sitting on a chair with a straight vertical back, with the elbow flexed 90° and the forearm in a neutral position and using the non-dominant hand [30]. The test was carried out in triplicate and the highest value obtained was recorded.

Body composition was assessed by bioelectrical impedance using the Biodynamics 450, analyzer with a current of 800 microamperes and 50 kHz. For the exam, the subjects, wearing light clothing, lay in dorsal decubitus on a gurney with a pair of electrodes positioned on the foot and another on the hand, both on the side opposite to the surgery for breast cancer [31]. Obesity was classified according to the cut-off points for fat mass proposed by Lohman et al. (1992) [29]. The subjects were tested after at least 5 h of fast, having practiced no vigorous physical activity in the last 12 h, having urinated 30 min before the beginning of the test and having abstained from alcoholic or caffeine-containing beverages for 24 h before the exam.

A blood sample was collected by venipuncture from the arm contralateral to the breast surgery after a 12 h fast for the determination of fasting glycemia. The reference value was that recommended by the 2014–2015 Brazilian Directives for Diabetes which considers <100 mg/dL as normal, > 100 to <126 mg/dL as reduced glucose tolerance, and  $\geq 126$  mg/dL as diabetes mellitus [32]. The same blood sample was used to determine the lipid profile using as reference the values proposed by the 5th Brazilian Directive of Dyslipidemia and Prevention of Atherosclerosis, i.e.: total cholesterol <200 mg/dL, LDL-cholesterol < 160 mg/dL, HDL-cholesterol  $\geq 50$  mg/dL, and triglycerides <150 mg/dL [33].

Blood pressure (BP) was measured with an Omron (HEM-7200) instrument of the Omron 7000 line. The reference values for pressure levels were those established by the Brazilian society of Cardiology in the 6th Brazilian Directives of Hypertension (2010), which define BP  $\geq 140/90$  mmHg as arterial hypertension. The measurement was made in triplicate on the arm contralateral to the surgical procedure and the mean of the last two values was considered to be the real BP [33].

MS is characterized by the association of several cardiovascular risk factors in the same individual and has been associated with an increased risk of breast cancer [34], as well as with coronary disease, stroke and peripheral vascular disease [35]. The syndrome is defined by the presence of visceral or centripetal obesity associated with changes in BP, lipid profile and insulin metabolism. There are different criteria for the definition of MS, such as those of the WHO [23], of the NCEP-ATP III) [24], revised in 2004, and of the IDF [25]. There is no consensus about the best definition of MS to be used and its diagnosis must include the presence of abdominal obesity as an essential condition, so this condition must be present plus 2 other criteria as defined, for example, by NCEP-ATP III, as shown in Table 1.

### 2.2. Statistical analysis

A descriptive analysis was carried out, resulting in frequency tables for the qualitative variables. The Fisher exact test was used to determine the relationship between the qualitative or nominal variables, and the nonparametric Mann-Whitney and Kruskal-Wallis tests were used to determine the relationship between continuous and categorical measures. All analyses were carried out with the aid of the IBM SPSS 20 (Statistical Package for the Social Sciences) e Excel 2010® (Microsoft Office) software considering a bidirectional  $\alpha$  of 0.05 and a 95% confidence interval.

## 3. Results

The sociodemographic characteristics of the sample under

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