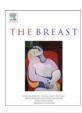


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Original article

Relationship between body mass index, waist circumference and waist to hip ratio and the steroid hormone receptor status in breast carcinoma of pre- and postmenopausal women

Rosilene Lima Pinheiro ^{a,b}, Luis Otavio Sarian ^{b,*}, Aarão Mendes Pinto-Neto ^b, Sirlei Morais ^b, Lucia Costa-Paiva ^b

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ABSTRACT

Objective: To assess whether body mass index (BMI), waist circumference (WC) and waist to hip ratio (WRH) are associated to the steroid receptor status in breast carcinomas.

Methods: Four hundred and seventy three women with breast malignancies stage I–III were included. Weight, height, the waist and hip circumferences (WC), body mass index (BMI), and the waist to hip ratio (WHR) were determined. The expression of estrogen (ER) and progesterone (PR) receptors was determined with immunohistochemistry.

Results: Most women had central obesity (WC \geq 88 and WHR \geq 0.85 in 64.3 and 73.4%, respectively). The majority (78.1%) of the women had tumors that expressed at least one of the HR. BMI, WC and WHP were not related to the HR status in neither the pre- or postmenopausal women. Multivariate analysis confirmed these findings.

Conclusions: BMI, WC or WHR may not be good predictors of HR status in breast malignancies in either pre- or postmenopausal women.

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Introduction

Multiple epidemiological lines of evidence have shown that nutritional and other lifestyle factors may affect the incidence of breast malignancies. In vivo and in vitro experimentations have assessed the role of steroid hormones to a large extent – with special emphasis to estrogen – in the etiology of breast cancer. These hormones are closely related to the growth regulation and differentiation of breast tissues. ²

One major investigational frontline is currently examining the etiological risk factors associated with breast cancers expressing different patterns of hormone receptors (HR). Firm epidemiological documentation shows that the pattern of HR expression may help discriminate tumors with markedly different epidemiological risk profiles, although many studies still treat breast malignancies, with different patterns of HR expression, without the necessary distinction.³ Several investigators have highlighted the fact that the etiological mechanisms of tumors that express estrogen receptors

Excess body adiposity is one of the major risk factors for breast cancer in postmenopausal women. It has long been shown that body fat affects the blood concentration of circulating estrogens through aromatase conversion of steroid precursors. More recently, the effects of these excess estrogens have been demonstrated in the breast. Have Hamman work work and between Hamman doesity (in most studies determined through the body mass index, BMI) have yielded conflicting results. For instance, several studies reported an increased incidence of positive Hamman breast malignancies in obese postmenopausal women, 4.5,8,14,16,19-21 whereas other important studies failed to demonstrate this relation. 15,18,23

It seems that part of these contradictory results may be ascribed to the studies' methodological flaws in ascertaining and characterizing obesity. It is known, for example, that abdominal adiposity is more important in terms of estrogen production than the fat stored in other body sites. Interestingly, excess abdominal fat was found to be related to a reduction in sex hormone binding proteins, thereby increasing the bioactivity of circulating estrogens. ^{24,25} Other body measurements that may be associated with the level of circulating estrogens are the waist circumference (WC) and the

E-mail address: paivaepaiva@uol.com (L. Costa-Paiva).

^a Section of Nutrition and Dietetics, National Cancer Institute (INCA), Rio de Janeiro, Brazil

^b Department of Obstetrics and Gynecology, Faculty of Medical Sciences, Universidade Estadual de Campinas, Campinas, São Paulo, Brazil

differ from those related to tumors that do not, with obvious epidemiological implications. $^{4-8}$

^{*} Corresponding author.

waist to hip ratio (WHR). These measurements have a confirmed association with other health problems, like diabetes mellitus and cardiovascular events. However, there is insufficient information about the association of these obesity parameters with the risk for breast cancer and the HR status of the tumors. 4,16,23

The present study aims at improving knowledge on the relation between the parameters (WC and WHR) used to define central obesity and the expression of HR in breast malignancies of pre- and postmenopausal women. These results may cast further insight into the actual behavior of estrogen production in obese women, providing a better discrimination of the body characteristics that may contribute additional risk for breast cancer.

Subjects and methods

Study population

This is a cross-sectional study on 473 women with breast malignancies stage I–III, treated at the National Cancer Institute, Brazil. The sample derived from the 1188 cases of unilateral breast cancer treated at the institution during the year 2004. 2004 was the last year for which data were considered suitable for the present study, because from 2005 onwards patients have been allotted to specific study protocols that may confer bias to the selection criteria. Exclusion criteria comprised: (i) clinical situations that might have affected the nutritional status, e.g. other types of cancer, gestation or HIV-positive; (ii) bilateral oophorectomy; (iii) impossibility to collect anthropometric data; and (iv) lack of data about the HR status.

Data collection

Clinical and epidemiological data were obtained from the patients' medical files: birth dates, race, educational level, smoking history, age at the diagnosis of the breast malignancy, family history of breast cancer, lactation, current or past use of oral contraceptives (OC), current and past use of hormone therapy (HT), menopausal status at the time of diagnosis. These data were used for multivariate adjustment of further analyses.

The anthropometric data were obtained at the admission visit, before the surgical procedure, with the techniques recommended by the World Health Organization 27 : weight was measured in kilograms (kg), with a Filizola scale with a precision to 100 g; height was measured in centimeters (cm) with an estadiometer coupled to the scale; the waist and hip circumferences were measured in centimeters with flexible and not extensible tapes. Body mass index (BMI) was calculated through the formula BMI = weight/(height^2), and the waist to hip ratio was the ratio of the waist circumference/hip circumference.

Senior breast surgeons carried out initial tumor staging in accordance with the TNM 5th edition. Tumor size, histological grade, lymph node compromise and HR determination were performed by INCA's Division of Pathology. For this study, only invasive breast carcinomas were included (lobular or ductal). The expression of HR (estrogen (ER) and progesterone (PR)) was determined with immunohistochemistry, and cases harboring more than 1% of stained nuclei were considered as positive. INCA's ethics review board approved the study protocol (protocol number 06/2005).

Data analysis

Data were recorded in Excel[®] spreadsheets and statistical calculations were performed using the R environment for statistical computing. Statistical significance was set to p = 0.05 and 95% confidence intervals (95%CI) were calculated where appropriate. Frequency tables were produced to describe the study

population. The thresholds used to determine obesity were those proposed by WHO (1997): (a) three categories for BMI: <25.0, 25.0-29.9 and $\ge 30.0 \text{ kg/m}^2$, (b) WC in two categories: <88 or >88 cm and (c) WHR in two categories: <0.85 or >0.85. The third category of BMI defined obesity and the latter categories of WC and WHR defined central obesity. For statistical purposes, HR status was grouped into four categories according to the specific estrogen (ER) and progesterone (PR) receptor statuses: (ER+/PR+. ER+/PR-, ER-/PR+ and ER-/PR-). Frequency comparisons were analyzed with Fisher's exact tests. Prevalence ratios (PrevR - for disambiguation with the progesterone receptor) were calculated to assess the differences in prevalence for HR within the categories for BMI, WC and WHR. The log-binomial method was used to further adjust PrevR and its 95%CI for age, race, years of formal education, smoking history, lactation, use of HT or OC, family history of breast cancer, menopausal status, age at menopause, clinical staging, tumor size, histological grade and lymph node status. The Fligner-Killeen test of homogeneity of variances was used prior to the multi-way analysis of variance (ANOVA) study of the differences in the mean values of BMI, WHR and WC across the HR status categories. In this multivariate model, p values were adjusted for age, tumor size, number of positive lymph nodes and histological grade.

Results

Table 1 summarizes the key clinical and epidemiological characteristics of the study population. The mean age at diagnosis of breast cancer was 58.8 years (DP \pm 13.8). Most patients were white (61%); postmenopausal (67.9%) – in postmenopausal women the

Table 1Key epidemiological characteristics of the women

| Characteristic | n | % |
|-----------------------------------|-----|------|
| Race | | |
| Not defined | 37 | |
| White | 266 | 61.0 |
| Non-white | 170 | 39.0 |
| Smoking history | | |
| Not defined | 6 | |
| Yes | 160 | 34.3 |
| No | 307 | 65.7 |
| Lactation | | |
| Not defined | 103 | |
| Yes | 319 | 86.2 |
| No | 51 | 13.8 |
| Family history of breast cancer | | |
| Not defined | 2 | |
| Yes | 127 | 27.0 |
| No | 344 | 73.0 |
| Menopausal status at diagnosis | | |
| Postmenopausal | 321 | 67.9 |
| Premenopausal | 152 | 32.1 |
| History of oral contraceptive use | | |
| Not defined | 43 | |
| Yes | 244 | 56.7 |
| No | 186 | 43.3 |
| History of hormone therapy | | |
| Not defined | 142 | |
| Yes | 41 | 12.4 |
| No | 290 | 87.6 |
| BMI (kg/m ²) | | |
| <25 | 147 | 31.1 |
| 25-29.9 | 194 | 41.0 |
| ≥30 | 132 | 27.9 |
| Waist circumference (cm) | | |
| <88 | 169 | 35.7 |
| ≥88 | 304 | 64.3 |
| Waist to hip ratio | | |
| <0.85 | 126 | 26.6 |
| ≥0.85 | 347 | 73.4 |

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