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RESEARCH ARTICLE

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HEIGHT ASSESSMENT AS A RISK FACTOR FOR BREAST CANCER IN BRAZILIAN WOMEN

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ABSTRACT

Objective: to evaluate the height of patients with and without breast cancer based on the national average height of Brazilian women, and to verify whether women who are taller than average are at increased risk. **Methods:** 100 patients attended at the Mastology outpatient clinic, and 100 patients attended at the Gynecological Endocrinology Outpatient Clinic were selected. From the data contained in their medical records, we obtained the heights of the 200 women who were grouped into the control group and the breast cancer group. **Results:** women with breast cancer, we found a mean of 1.59m in height, age from 28 to 97 years, whereas among the control group patients, the mean height was 1.55m, age ranging from 43 to 73 years. For these analyses, we use the ROC curve and logistic regression, which also showed a height cutoff point of 1.55m, above which there is an increased risk for breast cancer, with 78% sensitivity, and 50% specificity. In addition, there is a 20% increased probability of risk for breast cancer for every 10cm of height gain. **Conclusion:** The results observed in this work reinforce those previously found in other studies, according to which the greater the height, the greater the risk factor for developing breast cancer.

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INTRODUCTION

Breast cancer is a disease related to multiple factors. Therefore, the identification of modifiable factors that could improve survival rates and prevention of this disease is the subject of numerous studies (Qian *et al.*, 2019). Research that analyses factors such as smoking, alcohol use, obesity, and other behavioral and environmental factors has shown an increase in cancer-related risk. On the other hand, carcinogenesis is known to be also linked to genetics, a factor that cannot be modified, and hence it is important to know the individual's innate factors in order for us to be able to understand them (INCA, 2020). Therefore, an adult individual's height is directly related to their genetics and also to some extent, to their external environment, which is why it has been studied extensively, since being taller is probably positively linked to having some specific types of cancer (Kabat *et al.*, 2013 a; b). Adult height is determined by the parents' height and is also an indicator of how the body has managed to develop according to external factors, such as diet and physical activity, and intrinsic influences, such as hormonal mechanisms (Ritte *et al.*, 2013). During childhood, the tissues of the human body are affected by substances such as insulin growth factor-1 [IGF-1], growth hormone [GH], estrogens, and androgens, and leptin-7 (Ritte *et al.*, 2013).

Such endocrinological interactions can vary in different ways in each individual and be influenced by environmental factors. Some studies lead one to believe that the positive association between greater height and increased risk of developing cancer could be related to the metabolic pathway, since these factors would underlie both the proliferation of breast cells and the overall growth of the human body (Ritte *et al.*, 2013). In some studies, height was analyzed in conjunction with some specific types of cancer, positive correlations having been found for breast, cervix, rectum, thyroid, skin, kidney, and endometrium cancer (Elands *et al.*, 2019; Kabat *et al.*, 2013 a). Each of breast cancer subtype exhibits different ways of progression, prognosis, and treatment. Because of this wide variation, research shows the statistically significant association between height and risk of breast cancer found in patients with positive estrogen and progesterone receptors. Nevertheless, this association was not statistically significant for breast cancer with negative receptors (van den Brandt *et al.*, 2021; Zhang *et al.*, 2015). In observing these data from the literature, one might think that the identification of single nucleotide polymorphisms associated with both height and cancer risk could help to elucidate this association (Kabat *et al.*, 2013a). This explanation would be beneficial at different moments in time I what concerns the disease is concerned: prevention, diagnosis, treatment, and prognosis. The aim is to verify the association between height and an increased risk of breast cancer and estimate the height value

that presents the greatest risk, based on the national average height and the height of women without breast cancer.

Sampling: The choice of patients was made at the Mastology and Endocrinological Gynecology outpatient clinics of the Department of Obstetrics and Gynecology at *Irmandade da Santa Casa de São Paulo (ISCMSp)*. One hundred patients diagnosed with breast cancer at the Mastology clinic and 100 patients without breast cancer at the Endocrinological Gynecology clinic were selected. The study was carried out between November 2017 and April 2018. Patients with the following conditions were excluded from the study: Pregnant women referred from the Endocrinologic and Mastology Gynecology outpatient clinic and women referred from the Endocrinologic Gynecology outpatient clinic having a history of breast cancer.

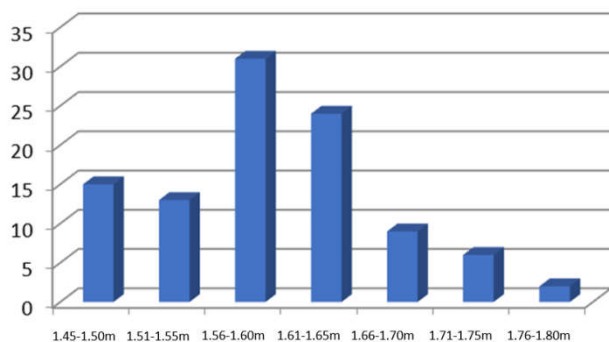
METHODS

This is a cross-sectional study with a control group, approved by the Ethics Committee for Research in Humans (*CAAE* permit No. 67138117.4.0000.5479 - 13 April 2017). A total of 101 treatment-naïve patients diagnosed with breast cancer at the Mastology Outpatient Clinic of the Department of Obstetrics and Gynecology at a hospital in São Paulo (SP), Brazil, and 100 control patients without the disease at the Endocrinologic Gynecology Outpatient Clinic of the same institution (visiting for routine follow-up or climacteric-related complaints) were selected. Then, the mean height and mean age of these women were calculated. The Survey on the female population's average height, for comparison between groups, was based on data from 2008-2009 collected by *IBGE* (the acronym for *Instituto Brasileiro de Geografia e Estatística*, i.e., the Brazilian Institute of Geography and Statistics) on the Brazilian women's mean height (Wirén *et al.*, 2014).

Statistical analysis: We carried out a descriptive analysis of the data found and the tabulation thereof. We used the SPSS program, version 13, to quantify the mean age and mean height of participants in both groups. The ROC curve was also adopted to verify the significance of differences in height, cutoff, sensitivity, and specificity of these parameters. To calculate the probability of developing cancer depending on height, logistic regression was used.

RESULTS

We considered 100 women diagnosed with breast cancer, and 100 women with no history of breast cancer diagnosis. The mean age of patients with breast cancer was 53.5 years (ranging from 28 to 78), whereas the mean age in the control group was 57.5 (ranging from 43 to 73), thus showing that the control group was comprised of slightly older women. In regard to mean height, the group of breast cancer patients had a value of 1.59 (ranging from 1.45 to 1.77), while the group of patients without cancer had a mean of 1.55 (ranging from 1.41 to 1.75), showing that women who had breast cancer were taller (Table 1).

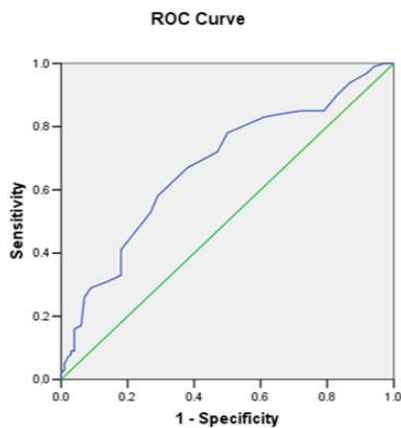


Graph 1. Distribution by height ranges of 100 women with breast cancer

Table 1. Analysis of the height and age variables of 100 patients with breast cancer and another 100 patients in the control group.

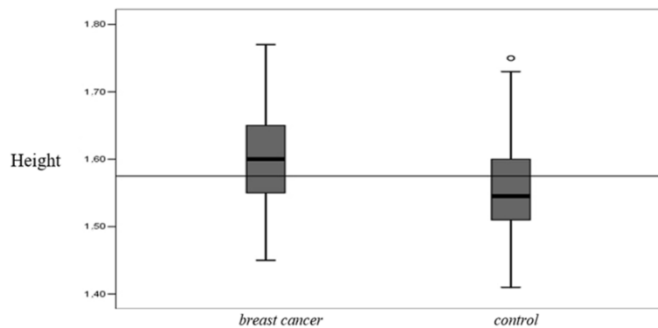
| | | Descriptives | | |
|---------------------|----------------|--------------------------------|-------------|------------|
| | Group | | Statistics | Std. Error |
| Age | With Cancer | Mean | 53.59 | 1.176 |
| | | 95% Confidence Interval — Mean | Lower Bound | 51.26 |
| | | | Upper Bound | 55.92 |
| | | 5% Trimmed Mean | 53.59 | |
| | | Median | 53.50 | |
| | | Variance | 138.204 | |
| | | Std. Deviation | 11.756 | |
| | | Minimum | 28 | |
| | | Maximum | 78 | |
| | | Range | 50 | |
| | | Interquartile Range | 16 | |
| | | Skewness | .004 | .241 |
| | | Kurtosis | -.399 | .478 |
| | Without Cancer | Mean | 58.29 | .606 |
| | | 95% Confidence Interval — Mean | Lower Bound | 57.09 |
| | | | Upper Bound | 59.49 |
| | | 5% Trimmed Mean | 58.12 | |
| | | Median | 57.50 | |
| | | Variance | 36.733 | |
| | | Std. Deviation | 6.061 | |
| Minimum | | 43 | | |
| Maximum | | 73 | | |
| Range | | 30 | | |
| Interquartile Range | | 8 | | |
| Skewness | | .530 | .241 | |
| Kurtosis | | .278 | .478 | |
| Height | With Cancer | Mean | 1.5961 | .00713 |
| | | 95% Confidence Interval — Mean | Lower Bound | 1.5819 |
| | | | Upper Bound | 1.6103 |
| | | 5% Trimmed Mean | 1.5946 | |
| | | Median | 1.6000 | |
| | | Variance | .005 | |
| | | Std. Deviation | .07135 | |
| | | Minimum | 1.45 | |
| | | Maximum | 1.77 | |
| | | Range | .32 | |
| | | Interquartile Range | .10 | |
| | | Skewness | .234 | .241 |
| | | Kurtosis | -.163 | .478 |
| | Without Cancer | Mean | 1.5541 | .00646 |
| | | 95% Confidence Interval — Mean | Lower Bound | 1.5413 |
| | | | Upper Bound | 1.5669 |
| | | 5% Trimmed Mean | 1.5520 | |
| | | Median | 1.5450 | |
| | | Variance | .004 | |
| | | Std. Deviation | .06456 | |
| Minimum | | 1.41 | | |
| Maximum | | 1.75 | | |
| Range | | .34 | | |
| Interquartile Range | | .09 | | |
| Skewness | | .501 | .241 | |
| Kurtosis | | .532 | .478 | |

The area under the curve test showed a value of 0.675, which means there is a greater number of breast cancer cases among taller patients. We could also find that the height of most women diagnosed with breast cancer ranged between 1.56 and 1.65. We show that the extremes values in this anthropometric data set did not correlate with a higher incidence (Graph 1). The ROC curve was used to analyze the significance of the difference in heights between the two groups. The area under the curve test had a value of 0.675, proving that taller patients have a greater number of cases breast cancer, with a $p < 0.001$. Based on this statistical analysis, we obtained a height cutoff point of 1.55, at which the risk of developing cancer starts increase (78% sensitivity, and 50% specificity). Therefore, this proved to be a test that could be used as a screening tool (Graph 2). The *IBGE* data revealed a national average height value of 1.575 m for the Brazilian female population, considering age groups above 25 years, which can be seen in Graph 4 as the black horizontal line at a value exceeding those of the two groups.



Graph 2. ROC curve in order to analyze the significance between the differences in height seen in the two groups

By comparing women with breast cancer who had an average height of 1.59 m with patients without breast cancer who had an average height of 1.554 m, we can see that the average Brazilian females' height is below the average of cancer patients (Graph 3).



Graph 3. Height distribution in the breast cancer group and control group as compared to the adult female population's mean height in Brazil

Finally, when using logistic regression to assess the probability of developing breast cancer, with height as the only risk factor, we concluded from using the formula $= \text{EXP}(BX)/(1+\text{EXP}(BX))$ that the risks of developing cancer having a height of 1.45, 1.55, and 1.65 are respectively 24%, 44%, and 66%. Therefore, we see a progressive increase in probability with increasing height.

DISCUSSION

Countless studies are still underway in order to provide better understanding of the factors involved with the development and progression of breast cancer. There already exists compelling evidence in the literature as to some risk factors acting as propellants of this type of carcinogenesis. However, there are some hypotheses that have not yet been really confirmed, such as the relationship between height and the development of different cancer types (Kabat *et al.*, 2013a, b). This work reveals that most women with breast cancer had heights between 1.56 to 1.60 m, an interval which contains both the national average height, which is 1.57 m, and the average height found in the control group at the clinic, which was 1.55 m. The average height of women with breast cancer (1.59 m) remains above the national average and that of female patients referred from the clinic at Santa Casa (Wirén *et al.*, 2014). By using the ROC curve, the specificity and sensitivity of the data of patients with and without breast cancer were established. The study was shown to be significant $P < 0.01$. It could be useful for screening patients at a higher risk. For this purpose, the best range would be the height from which there appear high sensitivity and moderate specificity. Values of 0.78 and 0.50, respectively, were observed. This height is shown by the ROC curve to be 1.55 m, i.e., women who are taller than that are at an increased risk of developing breast

cancer. This data has not been fully established in previous works, which generally did not demonstrate a cut off value for height. Accordingly, by using a significant patient sample, we managed to obtain a very diverse population, encompassing not only different ethnicities, but also cultural and genetic differences. In comparing women with breast cancer, we obtained a mean height of 1.59, whereas the mean in patients without breast cancer was 1.554 m, showing an average height greater than 2 cm than the national average for cancer patients and 4 cm below the national average for patients without breast cancer. Our research also yielded another important piece of data, given that we calculated the logistic regression by using only height as a risk factor, thus establishing that the taller the person, the greater their probability of having cancer. This data can be compared with other studies which showed that, for example, for every 10 centimeters of increase in height, the risk of cancer increases 15% (Ritte *et al.*, 2013). In another study, in turn, it was established that for every 10 centimeters of increase in height, the risk increases 20% (Kabat *et al.*, 2013b). A study comparing 2 groups, one with cancer and one without cancer, established 24% more risk for the tallest group (Kabat *et al.*, 2013a). A 5 cm increase in height cm was also associated with a higher risk of cancer mortality in women with an RR of 1.03 (95% CI 1.01-1.16), and in men with an RR 1.03 (CI 95 % 1.01-1.05), thereby showing, once again, a harmful influence from height in cancer progression (IBGE, 2021). Hypotheses about the association between height and the development of breast cancer may be genetically linked, in addition to the hormonal factors that influence growth.

CONCLUSION

This study focused on quantifying the height of women who had cancer and women without this disease and comparing the two data sets. We observed that the taller a woman, the greater her risk of developing breast cancer. Nonetheless, further studies are still needed for establishing relationships for conducting a better clinical follow-up of women who are known to be at a high risk and refining screening indicators, all of which could produce a positive impact on public health.

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