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False positive result in mammography and its association with the presence of obesity: a case-control study

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Abstract

Objective: *To analyze the association between a false positive result in mammography and obesity, inside the breast cancer early detection program in women affiliated to the Institute of Security and Social Services for Government and Municipality workers of the State of Baja California (ISSSTECALI).* **Material and methods:** *A case-control, retrospective study was done in women affiliated to ISSSTECALI to whom a mammography was performed between 2009 and 2012. Women with a false positive result in mammography were included as cases. Controls were women with a true negative result in mammography. Three controls were randomly selected for each case. Obesity was established with the body mass index (BMI) consigned in the woman's clinical file. Age and estrogen replacement therapy were included as co-variables.* **Results:** *Seventy nine cases were identified and 237 controls were included. Obesity was observed in 54.4% of cases and in 41.3% of controls (odds ratio: 1.69; 95% confidence interval for odds ratio: 1.01-2.82; p value: 0.043). A logistic regression model including covariables maintained the observed association (p = .044). No association was found with analyzed co-variables.* **Conclusions:** *A false positive result in mammography was associated with the presence of obesity.* (Gac Med Mex. 2016;152:453-6)

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Introduction

Obesity is considered to be a risk factor for the development of breast cancer[1], particularly morbid obesity[2]. Obesity has also been linked to mammographic inaccuracy, with the presence of false-positive results standing out[3], i.e., the possibility of a person free of the disease yielding a positive result in the test[4].

In our country, breast cancer incidence in 2008 was 14.63 cases for every 100 thousand women. The highest incidence occurs in Distrito Federal (45.84), followed by Sinaloa (45.76) and San Luis Potosí (45.20); conversely, the lowest incidence is observed in Estado de México (4.62), Chiapas (4.24) and Tlaxcala (2.96). The state of Baja California was at 12th place with a total of 19.72 cases per 100,000 women[5]. Breast cancer-related mortality rate in Mexico is 9 deaths for every 100,000 women. Today, it is the cause of a higher number of total deaths among Mexican women, affecting both younger and older women[6]. On the other hand, obesity in women is also very common. In 2012, 35.2% of female adult population in Mexico was affected by this condition[7].

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Table 1. BI-RADS classification for mammography interpretation

Category 0	Radiography insufficient, need for additional assessment with other study.
Category 1	Mammography negative to malignancy, without lymph nodes or calcifications.
Category 2	Mammography negative to malignancy, but with benign findings.
Category 3	Result probably benign, but requiring control at 6 months.
Category 4	Result suspicious of malignancy. Histopathological confirmation required.
Category 5	High suspicion of malignancy. Biopsy required confirming diagnosis.
Category 6	Biopsy-confirmed malignancy.

Mammography is the most important tool for breast cancer early detection[8]; it is used both as a tool for symptomatic patients' examination and for screening examination[9]. In our country, 2.1 million women had a mammography practiced during the year 2012[7]. For the identification of results, the American College of Radiology Breast Imaging Report and Database System (BI-RADS) is used[10]. The BI-RADS system categories are shown in table 1.

False-positive results are common in mammography. It is estimated that up to one third part of women who are evaluated for a period of 10 years will have at least one false-positive result[11]. Obese women appear to be at higher risk for false-positive results[12].

The importance of obtaining a false-positive result lies in that it might lead to poor adherence to the screening program with avoidance of subsequent mammographic studies[13], in addition to the psychological impact such as the anxiety experienced by these women, which might last for at least one year[14]. A study conducted in Denmark points out that inner peace and existential values such as pessimist thoughts about the future and less sense of wellbeing are equally significant within the first half of the year after final diagnosis for women with breast cancer and for women who received false-positive results, feelings that may last for up to 3 years[15]. It is important for doctors to inform their patients on the possible risk for obtaining a false-positive result[16].

In the present work, the association of a mammography false-positive result and the presence of obesity is assessed in women who had mammographies practiced within the ISSSTECALI breast cancer opportune detection program during the 2009-2012 period. In this institution, an average of 60,000 women are annually attended to, with 27,000 of these women at ages of 40 or more years, and an average of 4,000 mammographies are practiced per year.

Material and methods

A case-control, secondary-sources, retrospective study was conducted. The study population was comprised by ISSTECALI affiliates who had a mammography practiced within the institution's breast cancer opportune detection program during the years 2009 through 2012.

To obtain the required information, the institute's informatics department was requested the mammography studies results of all patients who underwent a mammography during the 2009-2012 period, where women with positive results were identified. All positive results were checked against the information contained in the medical file to identify true positive results and those that turned out to be false-positive. Women with mammography false-positive results comprised the group of cases. Identification of cases required: 1) having a mammography positive result for cancer (BI-RADS 4 or 5); 2) cancer-negative histopathological study, and 3) information on age, use of estrogen replacement therapy, weight and height or BMI available in the medical file.

Each time a case was identified, three controls were randomly selected from the same source. Identification of controls required: 1) having a cancer-negative mammography result (BI-RADS 1, 2 or 3); 2) absence of a breast cancer diagnosis until the last medical assessment and 3) information on age, use of estrogen replacement therapy, weight and height or BMI available in the medical file. If a patient underwent a mammography more than once during the investigation period, a single measurement was randomly selected.

Both in cases and controls, the age, estrogen replacement therapy and BMI co-variables were also searched for. The age that was taken into account was the one reported at the moment of the mammography. Estrogen replacement therapy was considered if there was exposure to replacement estrogens in menopausal women for at least 2 years prior to the mammography. BMI was calculated based on the patient's weight and height, with BMI ≥ 30 being categorized as obesity. The anthropometric

Table 2. Main characteristics observed among cases and controls

Variable		Cases n (%)	Controls n (%)	OR (95% CI)	p*
Age	< 60 years	17 (21.5)	52 (21.9)	Ref. group	
	≥ 60 years	62 (78.5)	185 (78.1)	0.97 (0.52-1.81)	0.937
Estrogen replacement therapy	Yes	4 (5.1)	14 (5.9)	Ref. group	
	No	75 (94.9)	223 (94.1)	0.85 (0.27-2.66)	0.779
Obesity	Yes	43 (54.4)	98 (41.4)	Ref. group	
	No	36 (45.6)	139 (58.6)	1.69 (1.01-2.82)	0.043

*p-value obtained with two-tailed Pearson's chi-square test and alpha value of .05.
n: sample size; OR: odds ratio; 95% CI: odds ratio 95% confidence interval; p: p-value.

Table 3. Logistic regression model

Variable	Estimator	Standard error	OR (95% CI)	p
Age	–0.101	0.322	0.90 (0.48-1.69)	0.754
Obesity	0.534	0.265	1.70 (1.01-2.86)	0.044
Estrogens	–0.056	0.202	0.946 (0.29-3.02)	0.925
Constant	–1.329	0.202	0.265	0.001

Model summary: R^2 Nagelkerke, 019, Cox and Snell .013.
OR: odds ratio; 95% CI: odds ratio 95% confidence interval; p: p-value.

measurements for BMI that were considered were those obtained on the closest date to the day the mammography was practiced.

Integrating one variable for the mammographic study quality or for breast density was not possible, since this information did not appear in the analyzed records.

For statistical analysis, the odds ratio (OR) with its 95% confidence interval (CI) was calculated, and proportions were compared with Pearson's chi-square test, with the analysis being made with a two-tailed alpha-value of .05. A multivariate logistic regression model that included the above-mentioned independent variables was also constructed. The SPSS statistical program, version 20 for Windows, was used.

Results

A total of 10,027 mammography interpretations performed during 2009-2012, which included 193 (1.9%) positive results (BI-RADS 4 or 5) and 8,868 (88.4%) negative results (BI-RADS 1, 2 or 3), were reviewed. The remaining 966 mammographies (9.6%) were classified as category 0, category 3/4, or unclassified and were not considered for the study.

Of the 193 studies reported as positive, 51 (26.4%) could be identified as true-positive and 79 (40.9%) as false-positive according to the subsequently performed histopathological analysis. In the remaining 63 positive results (32.8%), no information was found in the medical files to classify them as true or false-positive. Once the false-positives or cases were identified, controls were randomly selected among the negative reports, at a ratio of 3 controls for each identified case.

Table 2 shows the main characteristics identified among cases and controls, where a larger proportion of obesity is appreciated in women with false-positive results than in controls with an OR: 1.69; 95% CI: 1.01-2.82; p = .043. Age and estrogen replacement therapy were not associated with false-positive results (p = .937 and .779, respectively).

The three studied independent variables were included in a logistic regression model, with the association observed between obesity and mammography false-positive result being maintained (p = .044). Table 3 shows the result obtained in the model.

Discussion

The results of the study showed that mammography false-positive results were associated with the presence of obesity, similar to reports from other studies where the weight of women undergoing mammographies was found to influence on the accuracy of the study, with an increased risk of false-positive result in women with obesity[3].

Age did not have any influence on the occurrence of a mammography with false-positive result, which is consistent with studies where age was not an important factor to predict the risk for a mammography false-positive result[17]. However, some authors have associated age as a determinant factor, especially in women aged 45 to 49 years[18].

With regard to estrogen replacement therapy, no association was found with the occurrence of mammography false-positive results ($p = 0.779$); however, other authors have found that receiving hormone replacement treatment is associated with an increased frequency of false-positive results, especially in postmenopausal women aged 50 years or more[18]. Another study refers that the effect of the use of hormone replacement treatment on the risk for false-positive results can persist for several years after the exposure ceases and, in users who did not discontinue it at the moment the mammography was performed, it might increase the risk of having to undergo biopsy[5].

Some limitations of the study are, in the first place, that it was a research of secondary sources and measurements could not be controlled by the investigators, who completely relied on the information reported in the medical files. Other important limitation was that there is no standardization in the institution for practicing and reporting mammographies, which precluded the possibility of including any measurement on the quality of the tests or breast density, although the study original design contemplated these measurements. Finally, the lack of histopathology reports in the medical files to corroborate the mammography result in women with a positive result hindered the identification of cases, with a selection bias possibly being generated.

With the results shown in this study, it can be concluded that there is association between a mammography false-positive result and the presence of obesity. Further prospective studies will be able to elucidate, with higher level of evidence, the causality of this association.

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