Mammographic Density as a Risk Factor for Breast Cancer in Women Above Forty Years

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ABSTRACT

The degree and pattern of density in a mammogram is a reflection of the amount and distribution of fibroglandular tissues in the breast. Mammographic density has been known to make breast cancer harder to detect but, lately, in addition to that, mammographic density has been found to be a risk factor for breast cancer. The aim of this work was to study this fairly new concept about mammographic density, as a risk factor for breast cancer. This is a retrospective study of 210 mammograms that demonstrated breast cancer. They were classified according to their degree of density following the BI-RADS classification. This study showed that breast cancers were 4.4 times more in dense mammograms than in hypodense ones among women above 40 years of age. This study reached results similar to the world literature that highly dense mammograms are risk factors for breast cancer, and hence women above the age of forty with dense mammograms need to have a regular breast follow up.

Key Words: Breast-Mammography-Density – Risk – Cancer.

INTRODUCTION

The radiographic appearance of the female breast varies among women because of differences in tissue composition; fat is radiographically lucent and appears dark on a mammogram, whereas connective and epithelial tissues are radiographically dense and appear light, an appearance described as mammographic density(I).

Mammographic density has been known to mask an already existing breast cancer(2) because a breast cancer has the same x-ray attenuation properties as the fibrogeandular breast tissue. That is why mammography alone was not commonly used to detect breast cancer in young women because their mammograms are usually dense.

There is now however, evidence that there is more to high density than the masking of tumors; mammographic density does not only mask cancers which may appear later but is actually a risk factor predicting the development of a new breast cancer(3,4,5,6).

The aim of this Work:

The aim of this work is to study this new concept of high mammographic density being a risk factor for breast cancer, especially among women after the age of forty, where normally their breasts appear less dense than women in younger age groups.

MATERIAL & METHODS

This is a retrospective study of 210 mammograms of breasts of women above the age of 40 years whose mammograms showed at least one malignant lesion.

Their ages ranged between 40 and 87 years with a median age of 58.5 years.

We focused on the age group above 40 years, because women at younger age normally have dense breasts in mammograms being in the child-bearing age. Whereas, women above the age of 40 have normally less dense mammographies.

The mammograms were from Kasr El Aini, Cairo University Hospital and to increase the number of mammograms studied, we reviewed more mammograms from the database of the University of Southern Florida.

These mammograms were reviewed for:

1. The degree, pattern and percentage of density using the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) classification (7):
RESULTS

All the 210 mammograms reviewed in this study showed breast cancer but the degree and pattern of density in them were found different when examined using the BI-RADS classification:

1- Thirty nine of the 210 (19%) were hypodense and mostly fatty and therefore, belonged to BI-RADS category 1.
2- Eighty four (48%) of mammograms showed scattered density and therefore, belonged to BI-RADS category 2.
3- Seventy (33%) of the mammograms showed homogeneous density and therefore, belonged to BI-RADS category 3.
4- Seventeen (8%) were found extremely dense and therefore, belonged to BI-RADS category 4.

Fig. (1): Malignant lesion in breast of high mammographic density BI-RADS 3

<table>
<thead>
<tr>
<th>BI-RADS Density</th>
<th>Category 1</th>
<th>Category 2</th>
<th>Category 3</th>
<th>Category 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of tumors</td>
<td>39 (19%)</td>
<td>84 (48%)</td>
<td>70 (33%)</td>
<td>17 (8%)</td>
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All the 210 mammograms studied had breast cancer but their degree and pattern of density were different: one hundred and seventy one (81%) of these mammograms showed different degrees of density but were all dense and belonged to B1-RADS categories 2, 3 and 4.

Only 39 (19%) of these mammograms showed practically no density and belonged to B1-RADS category 1. So breast cancer occurred 4.4 times more in dense mammograms than in hypodense ones.

DISCUSSION

The female breast is composed of fat on the one hand and connective and epithelial tissues on the other hand. Depending on the relative amounts of fat and connective and epithelial tissues present, the radiological appearance of the female breast varies from woman to woman;
variations in the mammographic density of breast tissue are referred to as parenchymal pattern of the breast.

Fat is radiologically translucent or clear (darker appearance), and both connective and epithelial tissues are radiologically dense (lighter appearance)(8).

Many studies have generally supported an association between parenchymal patterns and breast cancer risk (greater risk with increasing densities).

According to Byng, Yaffe and coworkers(9) there is considerable evidence that the mammographic density of the breast is one of the strongest risk factors for breast carcinoma. Women with a high breast density of 75% or more have a nearly 5-fold increased risk for breast cancer compared with women with a low density of less than 10% (1).

How can the highly dense mammogram be a risk factor for breast cancer?

1- It may be masking an already existing cancer and thus, delaying its diagnosis to a later date. Boyd and Colleagues (10) found that the risk for breast cancer in women with high breast density is markedly increased (by 17 fold) in the 12 months after a dense mammogram but negative for cancer. They think that, since this 17-fold increase in breast cancer is apparently limited to the 12 months after a screening examination, the high breast density masks, rather than encourages rapid growth of the tumor and leads to false negative mammograms.

2- Kerlikowske(11) suggests that there is more to high density than the masking of tumors; there might be a biologic connection between dense breast tissue and breast cancer. In favour of this possibility is that this association between breast cancer and extensive mammographic density is observed even when the density was observed as long as 8 years before the diagnosis of breast cancer

3- The mammographic density of the breast seems to provide an index of cumulative exposure to the current and past hormonal and reproductive events that influence the incidence of breast cancer(12). Density represents epithelial tissue and fibrosis thus growth factors that stimulate cancers may be produced in this histological environment. Mammographic density is associated with increased tissue cellularity and increased growth factors, such as insulin growth factor(13) that may promote cancer growth.

The value and importance of the highly dense mammogram:

This fairly new discovery about mammographic density, being a strong risk factor for breast cancer has important consequences.

1- Any woman whose mammogram is highly dense should be re-examined and then followed closely; and because a dense mammogram may be masking breast cancer, mammography alone would not be enough for examination and follow up. Digital mammography, sonomammography or even magnetic resonance imaging should be used for early diagnosis of breast cancer.

2- This finding may lead to a better understanding of the factors that cause breast cancer and to new approaches to prevention of the disease. This is because the changes occurring in the mammograms reflect the changes occurring in the developing cancer in the breast and these radiological features can be observed and measured and can be related directly to risk of breast cancer and are likely to be of value in research into the etiology of breast cancer.

According to Beryd, Martin et al.,(14), since all risk factors for breast cancer, including genetic and environmental factors must ultimately exert their influence by an effect on the breast increasing the number of cells and the quantity of collagen in the breast and thus, increasing the mammographic density. And since some of these influences include endogenous and exogenous hormones and the menopause, a better understanding of the factors that influence the response of the breast tissue to these hormonal exposures may lead to an improved understanding of the etiology of mammographic density and of breast cancer.

This study of 210 malignant mammograms 171(81%) of the tumors occurred in the dense mammograms (BI-RADS categories 2, 3 and 4) and only 39 (19%) were found in the hypodense mammograms of BI-RADS category one. This
means that breast cancers occurred in dense mammograms 4.4 times more than in hypodense mammograms.

This finding is in accordance with most of the authors in the world literature. **Yaffe, Boyd and Coworkers**\(^{(15)}\) found that a density of 75% or more of the mammogram carry a risk for cancer 4-6 times than the risk of mammograms with an absence of density. **Boyd, Rommens, et al.**\(^{(16)}\) found that mammographic density is a strong risk factor for breast cancer, and that risk of breast cancer is 4-5 times greater in women with density in more than 75% of the breast than in women with little or no density in the breast.

**Fait and Zizka**\(^{(17)}\) found that mammographic density increases during hormone replacement therapy but this increase is not identical with the enhanced mammographic density which is a risk factor for breast cancer. The mammographic density associated with the hormonal treatment recedes within 14 days after its withdrawal. **Byrne, Schaier et al.**\(^{(18)}\) reached the conclusion that high-density mammographic parenchymal patterns, as measured by the proportion of breast area composed of epithelial and stromal tissue, had the greatest impact on breast cancer risk. In their study 28% of the breast cancers were attributable to having 50% or greater breast density.

This study was done to check if dense mammography is a risk and a predictive factor for breast cancer in women above the age of forty, and it proved that it is.

More work will be done in a prospective study to find the relationship between dense mammography as a risk factor and other known risk factors for breast cancer such as a positive family history, age, previous or concurrent cancer in the other breast.

**Conclusion:**

The degree of density of a mammogram reflects the amount of epithelial tissue and fibrosis in the breast; breasts which are mainly fatty are hypodense but breasts with more fibroglandular tissue are dense.

Mammographic density is a predictive factor to breast cancer because it may mask an already present cancer which will appear later when it reaches a bigger size and also because the fibro glandular tissue causing the density may contain certain growth factors which enhance the development of cancer.

This work is a retrospective study of 210 mammograms showing breast cancer in all of them. They were reviewed for their degree and pattern of density using the BI-RADS classification. One hundred and seventy one (81%) of them were found to be dense and belonged to BI-RADS categories 2, 3 and 4 while only 39 (19%) were found to be hypodense and belonged to BI-RADS category 1.

This shows that breast cancer occurred 4.4 times in dense mammograms than in hypodense ones suggesting the fact that a dense mammogram should be considered a risk and even a predictive factor for breast cancer. And hence women above 40 years with dense mammograms need to do regular breast follow up by physical examination and mammography.

**REFERENCES**


