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MAMMOGRAPHIC DENSITY AND THE RISK AND DETECTION OF BREAST CANCER

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Abstract

With the increase in breast cancer risk over the years, there are many factors estimated that lead to it. However, till date which factor is majorly involved in development of breast cancer or which factor accounts more is not clearly evident. Mammography technique accounting for 80-90% of cancer being detected is believed to be the best method of detection. While mammographic density is manifested by increased proliferation of fat, stoma, epithelium and connective tissue, it is considered to be a risk factor for development of breast cancer. The current study was thus conducted to find out whether the mammographic density is actually a risk factor for development of breast cancer and to find out the better detection tool available. For this, the methodology adopted was review of various journals and studies already published with respect to mammographic density and its risk on development of breast cancer. The conclusion of the current study as well as from another comparable study was that the frequency of screening might be dependent on breast density and in such cases diagnostic techniques such as "digital mammography, ultra sonography and magnetic resonance imaging" may prove to be better detection tools. Moreover, recent studies have also suggested that mammographic density as a marker for risk of developing breast cancer holds true however, this fact needs to be evaluated further.

Keywords

Breast Cancer, Mammographic Density, Breast Density, Breast Imaging Reporting and Data System (BI-RADS), Mammography

1. Introduction

Breast cancer risk has been increasing over the years and there are many factors estimated that lead to it. Such factors include nulliparity, late menopause, age, ethnicity, hormonal factors, lifestyle factors, family history, use of hormone replacement therapy and the recent one being mammographic density (Society, 2007). However, till date there is no clear evidence that which factor accounts more or which factor is majorly involved in development of breast cancer. Mammography technique is believed to be the best method of detection and it accounts for 80-90% of cancer being detected (Society, 2007) . However, some cases of breast cancer have been arising which were not detected by standard mammography technique and it was observed that the failure in detection was due to high density of breast tissue in such cases which added a masking effect on the detection (Society, 2007).

2. Mammographic Density as a Risk Factor for Development of Breast Cancer

Mammographic density is manifested by increased proliferation of fat, stoma, epitheliumand connective tissue and is considered to be a risk factor for development of breast cancer (Kerlikowske, et al., 2007)(Jeffrey, Steven, Smith-Bindman, Ichikawa, MS, & al, 2008)(Vachon, et al., 2007)(Attam, Kaur, Saha, & Bhargava, 2008). This may take place due to some cell division stimulating growth factors or due to hormone exposure (Vachon, et al., 2007). These growth factors and hormones include “tamoxifen, menopausal hormones and insulin like growth factors – 1(IGF-1)” (Vachon, et al., 2007). Moreover, detection of breast cancer can be hindered by high breast density which may increase breast cancer development risk since it will remain undiagnosed. Therefore, there was a need to conduct studies in order to validate such known facts. In order to do this, this case control study having 1112 matched case control pairs was carried out. The study focussed on developing a relation between risk of development of breast cancer and percentage of density in the mammogram measured at baseline, according to the method of cancer detection.

The data used in the study was taken from three case control studies, "NationalBreast Screening Study (NBSS), Screening Mammography Program of British Columbia (SMPBC) and Ontario Breast Screening Program (OBSP)". The NBSS and OBSP took into account physical examination as well as mammographic screening in a randomized manner for screening the population whereas the SMPBC screened the population only through mammography.

On the other hand, a similar study done after this study compiled the data collected from seven mammographic registries who took part in the Breast Cancer Surveillance Consortium which was supported by National Cancer Institute during the study period and they were: "San Francisco Mammography Registry, Group Health's Breast Cancer Surveillance, Colorado Mammography Advocacy Project, Vermont Breast Cancer Surveillance System, New Hampshire Mammography Network, Carolina Mammography Registry, and New Mexico Mammography Registry"(Kerlikowske, et al., 2007).

The involvement of seven registries in the study aided in better understanding of the relationship between percentage density of mammogram and the associated risk of breast cancer with it due to large population participation with varied demographic characteristics which was lacking in the given study. Only 1112 invasive breast cancer patients were enrolled in the given study on the basis of verification through histological tests and they were classified as women of age ≤ 56years or > 56 years, whereas a similar study done in the year 2008 included 1,095,484 women age 35 years or older who underwent at least 1 mammogram in which breast density was measured through Breast Imaging Reporting and Data System (BI-RADS) (Jeffrey, Steven, Smith-Bindman, Ichikawa, MS, & al, 2008). However, the patient number was relatively good in comparison to other studies done after this study which included 372 women aged 50 years or older, done between 1997 till 2001 and this study included subjects who underwent at least 2 mammographic examinations and took subjects who lived in a defined area of the clinic (Vachon, et al., 2007).

This might have been a reason for low number of subjects in the study, so taking subjects from a limited area became a drawback of the study (Vachon, et al., 2007). In contrast to these, another study included 123 women of age more than 35years, done from April 2004 till March 2005 (Attam, Kaur, Saha, & Bhargava, 2008). The cases were selected for the study on the basis of biopsy only (Attam, Kaur, Saha, & Bhargava, 2008). After the first screening examination, the women who developed breast cancer in less than 12 months were excluded

from the given study. On the other hand, women having breast cancer before first screening, women who underwent breast implants as well as women who developed breast cancer within first 6months of follow up were excluded in a similar study (Jeffrey, Steven, Smith-Bindman, Ichikawa, MS, & al, 2008). This lead to inclusion of minimum number of cancer patients diagnosed through mammogram. An informed consent was taken from all the participants of the study, however, there is no term mentioning a certificate of confidentiality as received in a similar study (Jeffrey, Steven, Smith-Bindman, Ichikawa, MS, & al, 2008). For estimation of risk factors, subjects were made to fill questionnaires containing "demographic characters, use or non use of hormone therapy and menstrual as well as reproductive risk factors".

3. Breast Cancer: Risk Factors

Whereas, another similar study made the subjects fill questionnaire containing menopausal status, history of breast cancer in first degree relatives, namely mother, sister or daughter, history of oophorectomy, age at first live birth and height and weight (Kerlikowske, et al., 2007). All these factors are very important in estimation of the breast cancer risk however, use of hormone therapy being another risk factor was not included. Mammographic density was estimated by taking computer assisted craniocaudal images and images were classified into either of the 6 classes ofdensity"0%, <10%, 10 to <25%, 25 to <50%, 50 to <75% and ≥75%"however, another gained an advantage on estimation by taking left and right mediolateraloblique (MLO) and left and right craniocaudal (CC) scans and then percentage of density as well as absolute density was calculated from these scans(Vachon, et al., 2007). However, the advantage in both the studies was that scans were given in random order for analysing without letting the observer know which scans were of controls and which scans were of cases.

This feature also aided in avoiding bias to a greater extent and thus, helped in generating well defined results. A number of statistical tests were performed in order to compare characteristics of cases and controls, namely, "paired t- test for symmetrically distributed continuous variables, Wilcoxon rank sum tests for continuous variables with skewed distribution and Mantel-Haenszel chi square tests for categorical variables". A two tailed test was used as well for calculating p-value. Moreover, conditional logistic regression was used

to analyzematched data and logistic regression for unmatched data and finally a Cochran–Armitage test was done to assess increased risk with greater density.

Whereas, a comparable study performed only unpaired t-test, chi square test and univariate logistic regression for statistical analysis (Attam, Kaur, Saha, & Bhargava, 2008). Therefore, the given study was able to provide a profound analysis of the data being collected and generated during the whole of the study period. The results suggested that "smaller number of live births, nulliparity, family history, later age at first birth, later age at menopause, use of hormone replacement therapy and high breast density" (odds ratio for those with density ≥75% was 5.7 at 95% confidence interval) were the most common factors prevailing amongst the cases. Also, it was found that the cases had 5.8 percent more dense mammogram taken as baseline than that of the control subjects.

Another study suggested that older age and non-Hispanic white race or ethnicity were also common in breast cancer patients (Jeffrey, Steven, Smith-Bindman, Ichikawa, MS, & al, 2008). Moreover, this study gave the result that younger women had higher correlation between cancer and breast density (Jeffrey, Steven, Smith-Bindman, Ichikawa, MS, & al, 2008).

Finally, the given study was able to clearly indicate that there is an association between risk of developing breast cancer and the mammographic density no matter how it was detected. This fact came out when it was seen that 26% of all breast cancer women of younger age and 50% of cancers detected in younger women within 12 months of screenings producing negative results were allied to breast density in ≥50% of mammograms.

On the other hand, a recent study suggested that besides these facts, there was elevated risk of developing breast cancer in pre-menopausal women as compared to postmenopausal women (Attam, Kaur, Saha, & Bhargava, 2008). Moreover, the study came out with a result that the risk endured for 8years following the study and this was majorly estimated in younger women and among these during the initial 2 years, the risk was much higher. The given study also proved through its results that breast density actually interfered with the cancer detection. However, a recent study gave the result that increased use of BI-RADS may be a causal factor for increased risk of breast cancer within 3 years (Kerlikowske, et al., 2007).

4. Findings and Conclusion

Ultimately, it is suggested from the given study as well as from another comparable study that frequency of screening might be dependent on breast density and in such cases diagnostic techniques such as "digital mammography, ultras onography and magnetic resonance imaging" may prove to be better detection tools (Attam, Kaur, Saha, & Bhargava, 2008). Moreover, recent studies also suggest that density is marker for risk of developing breast cancerhowever, this fact needs to be evaluated further (Vachon, et al., 2007) and better prediction of risk of breast cancer can be done by performing BI-RADS examination comprising of two longitudinal measures instead of single measure.

Moreover, breast cancer risk can be predicted for 5 years in case breast density is routinely measured (Jeffrey, Steven, Smith-Bindman, Ichikawa, MS, & al, 2008). Besides all these proven facts from the respective studies, there is a need to validate their accuracy before they can be applied in clinical practice for estimation of the risk.

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