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Implications of age in mammographic density interpretation

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Highlights

- **The age of the women is related inversely with breast density.**
- **Breast density is related positively to breast cancer**
- **Restriction of the Mammography sensitivity as a screening tool for breast cancer with increasing breast density**
- **Adding imaging modalities to screening Mammography like USS and MRI especially in a high-risk patient for breast cancer who have dense breasts.**

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ABSTRACT

Objective. The importance of breast density correlated with its significant impaction in Mammogram's interpretation and to the increased risk of development of breast cancer, we examined the breast density of 1051 of screening and diagnostic Mammography in Mammography unit in Benghazi medical center, our study aimed to find the relationship between the age and mammographic breast density.

Materials and Methods. This is a retrospective review of the diagnostic and screening Mammography underwent in Benghazi Medical Center's in Mammography unit during 2016-2917. Analysis of variance and descriptive analyses were used to evaluate the relationship between patient age and breast density.

Results. A total of 1051 women were examined by digital mammography at Department of Radiology in Benghazi Medical Center during the period from 2016-2017, the women age was ranged from 22 to 88 years with a median age of 48 years, the subgroups are Classified by the age decade, and we find that the relationship between the age and the breast density is significant inverse relation (p=0.000) 60.9% of patients between40 and 49 years old had dense breasts. and it reduced to 36.6% of women in their 50s. However, 28.7% of females in their 60s and 5.3% of patients in their 70s had dense breasts as interpreted on their screening and diagnostic mammograms.

Conclusion. We found that the age of the patient and the breast density are related inversely, but the interest is that we also found extreme value at the extremes of age where a considerable percentage of young women had mostly fatty tissue rather than glandular tissue and at the same time there's also a meaningful group of old women has dense breast tissue instead of fatty tissue.

1. Introduction

As the Breast density increase, the sensitivity of Mammography decreases in early diagnosis of breast cancer. Breast density is important in assessing the potential utility of supplementary imaging modalities for the diagnosis of breast cancer and screening it that is significant for the women, which are exposed to a high level of danger of breast cancer development. In addition to the relative amount of different types of breast tissue as seen on a mammogram (breast density), numerous risk factors are detected such as personal and family history of breast cancer. The scientists specified breast density as a new independent risk factor for breast cancer. Mammographic breast density reflects varying amounts of fat (dark areas on mammograms) and stromal and epithelial tissues (white areas on mammograms) in the breast. However, the breast density is considered as the absolute amount of dense or white areas in the breast (dense area) or a proportion of the mammogram that is composed of dense tissue (percent density). The dependence of mammographic breast density and patient age was found to be inversely related. However, we also found that the extreme value at the extremes of age, where a considerable proportion of young female had almost fatty breast tissue and evident dense breast tissue where found in a meaningful group of old age female When the breast density is increased the sensitivity of mammography is decreased in diagnosing the breast cancer. It was founded that increase Mammographic density is the commitment to an increase of four to six-fold in a woman's risk of evolving breast cancer (Byng *et al*., 1998; Vacon *et al*., 2007; Schreere *et al*., 2009; Pinsky and Hevie, 2010; Boyd *et al*., 2007).

The relation between breast density and increase risk of breast Malignancy was first outlined by Wolfe (1976) who calcified mammographic density according to qualitative parenchymal forms: N1 (fat), P1 (parenchymal thickening and ductal prominence mainly in a retro areolar region with <quarter of the breast involved ductal prominence), P2 (ductal and fibroglandular prominence with >quarter of breast volume), and DY (extensive dysplasia). Wolfe (1976) concluded a positive relationship between the risk of developing and breast cancer and dense tissue.

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Moreover, he noted that the N1 pattern had the minimum risk while the DY pattern had the maximum risk for breast cancer followed BY BI-RADS; Which initiate the standardize Mammographic reported qualitative Mammographic density descriptors, and are classified according to the following classes: class 1, predominantly fatty; class 2, scattered fibro glandular densities; class 3, heterogeneously dense; and class 4, extremely dense. These classes are followed by the addition of Quantitative value by the American College of Radiology, 2003 (ACR) which corresponds to the four outlines of Wolfe's classification. By this retrospective study, we intend to find out the dependence of the age on breast density, which may have a value in age-specific and risk-specific guidelines in breast cancer diagnosis and screening.

2. Materials and Methods

A retrospective review of screening and diagnostic mammography was conducted at the Mammographic unit at Benghazi Medical Center in 2016-2017. All mammography was performed with a digital technique using MAMMOMAT. Siemens, the Mammogram was examined by Radiologists with at least 20 years of experience. The Mammographic density is classified depending on ACR's BI-RADS to 4 classes. We reduce the inter-reader inconsistency of qualitative breast density through our special training and highly experienced breast imaging, we used the descriptive and inferential analyses to study the relationship between the female age and the breast density, and we performed the variance analysis with female age as a continuous variable to reach the importance of linear association. We have used SPSS software, ver. 23 in performing our analysis.

3. Result

A total of 1051 women were imaged by digital mammography at the Department of Radiology in Benghazi Medical Center in two years period from 2016 to 2017. The women's age was ranged from 22 to 88 years with a median age of 48 years, Fig. 1 shows the distribution of the women according to their age groups, and we found the most frequent age group is 40-49 years (49.1%), 62 (5.9%) women were less than 40 years, only 5(0.5%) of the women were 80 years or above, 328(31.2%) were 50-59 years, 121 (11.5%) women were 60-69 years and 19 (1.8%) women were70-79 years.

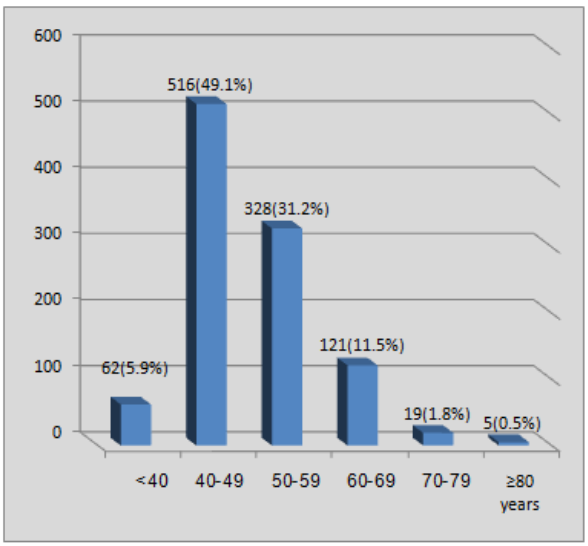

Fig. 1. Distribution of the women according to their age groups.

Fig. 2. shows the distribution of women by the degree of their breast density. There was 217 women (21%) with class 1 density (predominantly fatty) on mammography, 327 (31%) with class 2 (scattered fibroglandular elements), 467(44%) with class 3 (heterogeneously dense), and 40 (4%) with class 4 (extremely dense).

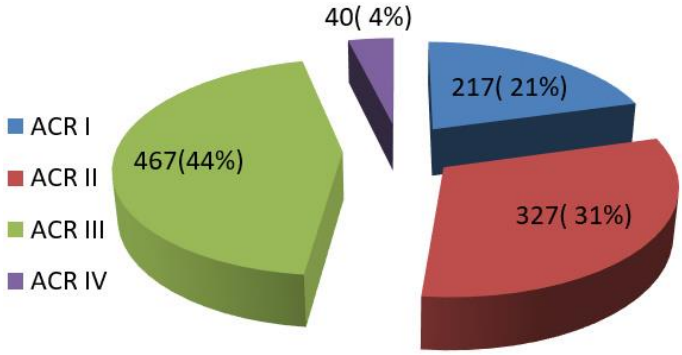

Fig. 2. Distribution of women by a degree of their breast density

The distribution of women according to their age and mammographic density is shown in Table 1 and Fig. 3.

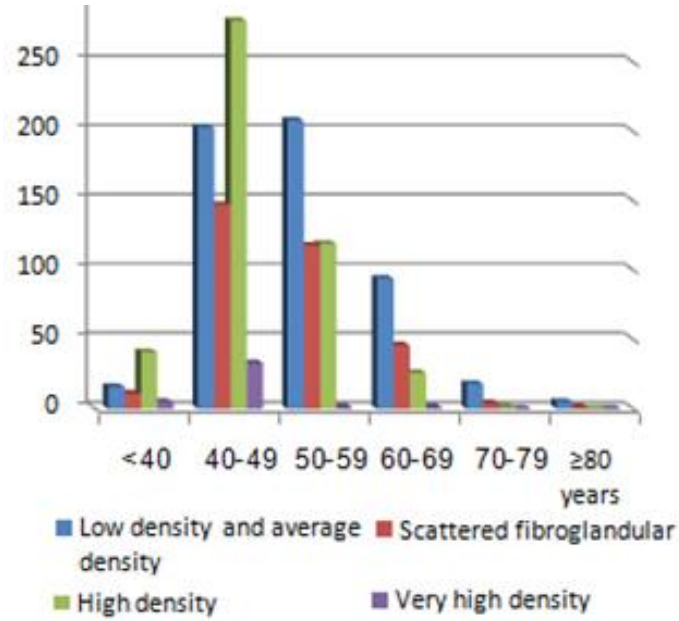

Fig. 3. Distribution of women by their age and classification of breast density.

Table 1

Mammographic density by age groups

Age group (years)	No. (%) of Patients in BI-RADS Density Categories				Total
	ACRI*	ACRII**	ACRIII***	ACRIV****	
<40 years	5	11	41	5	62
40-49	56	147	280	33	516
50-59	90	118	119	1	328
60-69	48	46	26	1	121
70-79	14	4	1	0	19
≥80 years	4	1	0	0	5
Total	217	327	467	40	1051

*Predominantly fatty (low density).

**Scattered fibroglandular densities (average density).

***Heterogeneously dense (high density).

****Extremely dense (very high density).

By using analysis of variance, there was a significant inverse relationship (P=0.000) between age and mammographic density, Fig. 4 and Fig. 5. A meaningful percentage of the younger female in this study had low and average-density tissue on mammography (25.8% of women 40 years old). As we predicted, most of the patients (54.5%) between the ages of 40 and 49 years had high-density breast tissue, and an extra 6.4% had very-high-density breasts. This parentage decreased to 36% high density and 0.3% very high density in women in their 50s. However, 28.7% of women in their 60s and 5.3% of women in their 70s had had high and very high

dense breast tissue. In our last group, no one of the women, 80 years old or older, and undertaking mammography had high dense or very dense tissue.

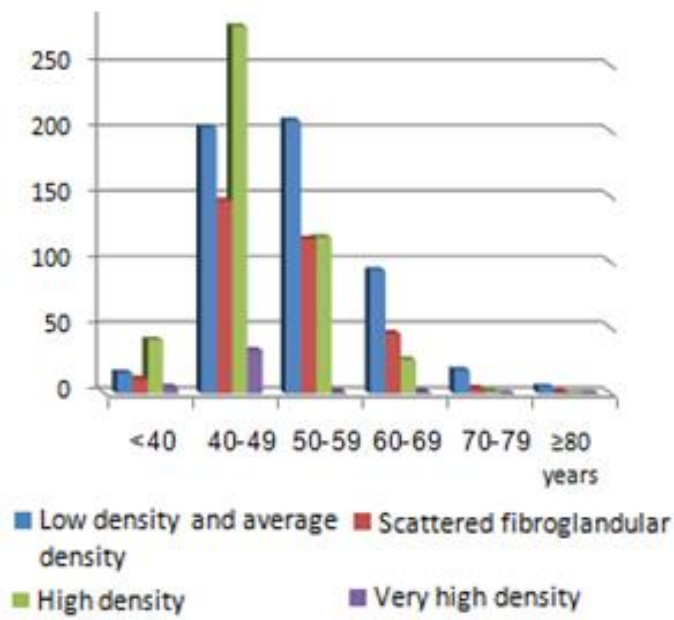

Fig. 4. Distribution of women by their age and categories of breast density

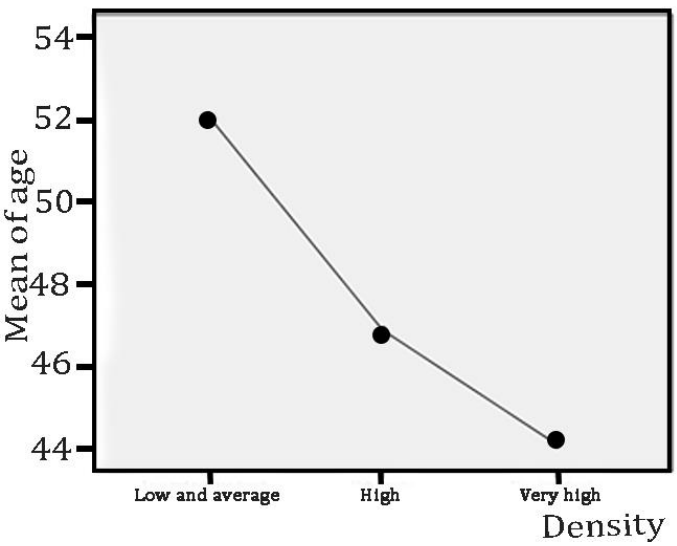

Fig. 5. Mean plots show the relationship between age and breast density.

Table 2

Distribution of women by age and categories of breast density

Age group (yrs)	Categories of breast density			Total
	Low & average	High	Very high	
<40	16 (25.8%)	41(66.1%)	5(8.1%)	62 (100%)
40-49	202 (39.1%)	281 (54.5%)	33 (6.4%)	516 (100%)
50-59	208 (63.4%)	119 (36.3%)	1(0.3%)	328 (100%)
60-69	95 (78.5%)	25 (20.7%)	1 (8%)	121 (100%)
70-79	18 (94.7%)	1 (5.3%)	0 (0%)	19 (100%)
≥80	5 (100%)	0 (0%)	0 (0%)	5 (100%)
Total	544 (51.8%)	467(44.4%)	40(3.8%)	1051 (100%)

The majority of the women (64%) had a usual or benign screening result, with routine yearly follow-up recommended. Of about 1051 screening mammograms, 116 (11%) were classified as BI-RADS category 4 with a recommendation for tissue sampling.

Table 3

BI-RADS results from screening mammography

BI-RADS categories	No.(%)	Recommendation
0	10 (1%)	Needs additional imaging
1	271 (25.8%)	Normal study; repeat mammography in 1 y
2	402 (38.2%)	Benign finding; repeat mammography in 1 y
3	212 (20.2%)	Needs short-interval follow-up; repeat mammography in 6 months
4	116 (11%)	Suspicious abnormality; biopsy recommended
5	38 (3.6%)	Highly suggestive of malignancy; biopsy recommended
6	2 (0.2%)	Biopsy proven Malignancy
Total	1051(100%)	

4. Discussion

We found a restriction of the Mammography sensitivity as screening tool for breast cancer with increased density and this mostly relevant to younger women. Moreover, we also found in our data a considerable percentage of old patient who still have dense breast tissue pattern in Mammography causing reduction in its sensitivity for breast cancer diagnosis. We notice that the age is not an accurate substitute for breast density resulting in considering breast density as an important factor in designing the breast cancer screening program especially in the patient who have other risk factors of breast cancer, the increase in breast cancer with age and decrease in breast density with age will be contradictory hence the breast cancer increase with the increase breast density as described by Wolf (1976). So according to that many study were done to find the factors which determine the pattern of breast density and so affecting the risk of breast cancer and they include the genes which control the differention of the ductal lobular unit and conversation of peripheral fat, exogenous hormone, breast feeding (Boyd *et al.*, 2005) also some study shows the breast density as heritable factor (Boyd *et al.*, 2009; Vachon, 2007) pike model of breast tissue ageing (Ginsburg *et al.*, 2008; Pike *et al.*, 1983) explain that the cumulative genetic damage sustained by breast epithelium rather than women chronologic age which may consider as the key in forming the tissue density, Mandelson *et al.* (2000) describe the decrease in mammographic sensitivity from 80% in fatty breast to 30% extreme dense breasts (Mandelson *et al.*, 2000).

Murphy *et al.* (2007) found that 78% of Mammographicall occult lesion was inpatient with heterogeneous or extremely dense breast, American College of Radiology Imaging Network (ACRIN)(Berg *et al.*, 2008), also study explain the advantage of adding ultrasound breast examination to Mammography inpatient with the dense breast which raises the sensitivity of each examination alone from 50% to 78% when performed together, also MRI, when added to Mammography in the evaluation of dense breast, increases the sensitivity of examination of Mammography from 33% alone to 80% with MRI (Kriege *et al.*, 2004). Sardanelli *et al.* (2004) showed significant statistical difference in sensitivity of Mammography and sensitivity of MRI in the dense breast from 66% in Mammography and 81% in MRI ., due to high cost and the psychological burden with the rate of false-positive finding in MRI it's used as a screening tool is restricted and only prefer to be utilized for the high-risk patient as mentioned BY Bleicher et al (Bleicher *et al.*, 2009).

Our study is agreed with a previous study (Cristina *et al.*, 2012) in that not only a proportion of old women had dense breast but also we find a meaningful subset of young women with fatty breast tissue, and these young women with the fatty breast tissue who have risk factors of developing breast cancer may not need the additional imaging modalities such as breast ultrasound and MRI which may be added to the screening mammography for uncovers mammographically occult malignancy.

5. Conclusion

Our data demonstrated that the relationship between patient age and mammographic breast density are related inversely. However, we also found Extreme values in the most extreme age, where a considerable portion of young females had almost fatty tissue and a meaningful group of older females had dense breasts. Increased density decreases the sensitivity of Mammography in early detection of breast cancer. Therefore, we documented that age is not a perfect substitute for breast density. Moreover, the women group with less dense breast (fatty breast) may not get any benefit from the additional imaging modalities, and we can consider the Mammography as the sufficient sensitive tool for early diagnosis of breast cancer in those females and at the same time, the meaning proportion of older women which have dense breast tissue will get the benefit of added imaging modalities to Mammography like USS and MRI especially in the high-risk patient for breast cancer.

Our goal is pointing for high light the need for guidelines for breast cancer screening which is Suitable for the age of the patient as well as breast density and the other risk factors of breast cancer and who might benefit from the added modalities.

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