

Mammogram density estimation as breast cancer risk in intermediate-risk women in Warith International Cancer Institution

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Abstract

Introduction: Breast cancer is the second most common malignant tumor worldwide and the leading cause of cancer death among women in developing regions, including the Middle East and North Africa. This study aims to evaluate Mammogram Density Estimation for Assessing Breast Cancer Risk in Intermediate-Risk Women at Warith International Cancer Institution.

Methods: The study included 261 women aged 40-78 who visited the Warith International Cancer Institution in Karbala, Iraq, between May 2023 and April 2024. Participants were divided into two groups based on mammographic breast density (MBD) according to the BI-RADS classification: non-dense (fatty and scattered fibroglandular) and dense (heterogeneously dense and dense) breasts. Demographic and clinical data were collected, and the association between breast density and various breast conditions was analyzed using logistic regression.

Results: For malignant cases, the odds ratio (OR) for invasive ductal carcinoma (IDC) was 1.04, suggesting no significant difference in the likelihood of IDC between dense and non-dense breasts. The OR for ductal carcinoma in situ (DCIS) was 1.60, indicating a slightly higher, but not statistically significant, likelihood of DCIS in dense breasts. The overall OR for malignant cases was 1.26, showing a trend towards a higher likelihood of malignancy in dense breasts, but it was not statistically significant.

For benign conditions, the OR for fibrocystic changes was 1.76, suggesting a higher likelihood in dense breasts, but the results were not statistically significant. Similarly, the ORs for fibroadenoma (1.27) and simple cysts (1.40) showed a slight increase in dense breasts but without statistical significance. Abscess and duct ectasia were less likely in dense breasts, but the results were not statistically significant.

Conclusion: The study findings suggest that some breast conditions may be more common in dense breasts, but the differences are not statistically significant in many cases. Further targeted research is needed to understand better the relationships between breast density and various breast pathologies.

Keywords: Colorectal Cancer; Breast Cancer; Family History; Association

1. Introduction

The burden of cancer is increasing worldwide, and poor survival from breast cancer is a direct consequence of the advanced stages of diagnosis prevalent in those places. This confirms the urgent need to strengthen strategies to combat breast cancer through the promotion of awareness of the importance of early detection of cancer, Examination, and

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appropriate treatment (1,2). In Iraq, breast cancer is currently the second main reason for the mortality rate among women after the formation of cardiovascular disease; 23% of deaths are related to cancer (3,4). In general, it is the most common malignancy among the general Iraqi population, and the number of registered cases is twice as high as those recorded for bronchogenic Cancer, the second most common type of cancer. The latest issues of Iraqi Cancer The registry shows that 4,115 cases of breast cancer were recorded among an estimated population of 32.5 million, accounting for 19.5% of newly diagnosed malignancies, 34% were female Cancers, and an incidence of 22 per 100,000 females (3). However, mammography is crucial for early breast cancer detection. Mammographic breast density (MBD) refers to the amount of dense tissue, including connective and glandular tissue, which appears white on a mammogram due to its hindrance to X-ray transmission. Fatty tissue appears darker as it allows X-ray passage. High MBD reduces mammographic sensitivity, masking potential cancers (5–7).

Increased breast density is a significant risk factor for breast cancer and reduces mammography's sensitivity and specificity. Breast cancer, characterized by abnormal breast cell growth, commonly presents as ductal or lobular carcinoma. MBD, determined by the relative amounts of breast fat and fibroglandular tissue, increases breast cancer risk by 4 to 6 times compared to non-dense tissue. Density is assessed using qualitative, quantitative, Wolfe classification, or BI-RADS density scores with digital technologies. Age, menopause, geography, and ethnicity influence breast density.(8–10).

1.1. Aim of the study

To evaluate mammogram density estimation of breast cancer risk in intermediate-risk women in Warith International Cancer Institution

2. Material and Methods

2.1. Study Population and Data Collection

The source population for this study consisted of women admitted to Warith International Cancer Institution in Karbala'a, Iraq, between May 2023 and April 2024. From the main study, 261 women aged 40 to 78 years with complete mammographic breast density (MBD) records were selected. Based on mammography results, the cases were categorized into two groups according to the BI-RADS classification for breast density (2013)

- Group I (Non-dense): Includes type A (fatty) and type B (scattered fibroglandular) tissues.

- Group II (Dense): This group includes type C (heterogeneously dense) and type D (dense) tissues. All subjects had comprehensive records in the center, including information on age, marital status, BMI (kg/m^2), and diagnosis.

2.2. Data Management and Statistical Analysis

The study included 261 patients presenting with breast lumps. Statistical analysis was conducted using IBM SPSS version 26. Participant characteristics were summarized using means, standard deviations, percentages, and tables. The association between different study parameters was tested using logistic regression. The fatty and scattered fibroglandular tissue categories were merged and used as the reference group.

3. Results

Table (1) illustrates a demographic comparison of dense vs. non-dense breasts, $n=261$, so we observe that age-dense breast tissue (ACR 3 & 4) is predominantly found in younger women aged 40-49, with 69 out of 137 dense cases (50.4%) in this age range. This supports existing research indicating that younger women are more likely to have denser breast tissue, which tends to become less dense with age. Non-dense breast tissue (ACR 2) is more prevalent in older women, particularly those aged 50-59 (29.8%) and 60-69 (23.4%). Most non-dense and dense cases are among married women (76.6% and 66.4%, respectively), reflecting the broader demographic patterns often observed in health studies where marital status can influence health outcomes and access to medical care. Single women comprise a more significant proportion of dense cases (13.1%) than non-dense cases (8.1%), which may relate to lifestyle or biological factors influencing breast density. Dense breast tissue cases are more frequently associated with higher Body Mass Index (BMI) categories, particularly among obese individuals (36.5%). This aligns with research suggesting a complex relationship between BMI and breast density, where higher BMI often correlates with increased breast density.

Table 1 Demographic Comparison of Dense vs. Non-Dense Breasts, n=261

Demographic Info	ACR(A)	% of Total Non-Dense	ACR (B)	% of Total Non-Dense	Total (non-dense)	ACR (C)	% of Total Dense	ACR (D)	% of Total Dense	Total (Dense)
Total Cases	0	0.0%	124	100.0%	124	123	89.8%	14	10.2%	137
Average Age	-	-	50.1	-	50.1	46.0	-	46.4	-	46.0
Age Range										
40-49	0	0.0%	51	41.1%	51	62	45.3%	7	5.1%	69
50-59	0	0.0%	37	29.8%	37	38	27.7%	5	3.6%	43
60-69	0	0.0%	29	23.4%	29	15	10.9%	2	1.5%	17
70+	0	0.0%	7	5.6%	7	8	5.8%	0	0.0%	8
Marital Status										
Single	0	0.0%	10	8.1%	10	18	13.1%	1	0.7%	19
Married	0	0.0%	95	76.6%	95	91	66.4%	10	7.3%	101
Divorced	0	0.0%	16	12.9%	16	8	5.8%	2	1.5%	10
Widow	0	0.0%	3	2.4%	3	6	4.4%	1	0.7%	7
Average BMI	-	-	27.2	-	27.2	28.2	-	28.0	-	28.2
BMI Range										
Underweight (<18.5)	0	0.0%	0	0.0%	0	0	0.0%	0	0.0%	0
Average Weight (18.5-24.9)	0	0.0%	32	25.8%	32	26	19.0%	4	2.9%	30
Overweight (25-29.9)	0	0.0%	59	47.6%	59	47	34.3%	5	3.6%	52
Obese (30+)	0	0.0%	33	26.6%	33	50	36.5%	5	3.6%	55

Table (2) provides a detailed comparison between non-dense (ACR 1 & 2) and dense (ACR 3 & 4) breast categories based on demographic factors such as age, marital status, and BMI. The odds ratios (OR) and their corresponding 95% confidence intervals (CI) help us understand the likelihood of having dense breasts to these factors. 40-49 age group Odds Ratio (OR): 2.36, 95% Confidence Interval (CI): 1.37 to 4.06 50-59 age group OR: 2.44, 95% CI: 1.37 to 4.31, 60-69 age group OR: 0.74 95% CI: 0.36 to 1.52, 70+ age group, OR: 1.51, 95% CI: 0.48 to 4.79, related with marital status, Single, OR: 2.39, 95% CI: 1.03 to 5.52, married OR: 1.00 (reference), divorced, OR: 0.59, 95% CI: 0.25 to 1.39, widow, OR: 2.21, 95% CI: 0.53 to 9.18, associated with BMI distribution, average weight (18.5-24.9), OR: 1.31, 95% CI: 0.69 to 2.50, Overweight (25-29.9) OR: 1.00 (reference), Obese (30+), OR: 1.98, 95% CI: 1.10 to 3.55. So, as an interpretation of these results, younger age groups (40-49 and 50-59) have significantly higher odds of having dense breasts compared to older age groups (60-69 and 70+). The odds of dense breasts decrease with age. Being single or widowed is associated with higher odds of having dense breasts compared to being married. Divorced individuals have lower odds of dense breasts compared to married individuals. Obesity is significantly associated with higher odds of dense breasts compared to being overweight. The average weight does not differ substantially from being overweight in breast density.

Table 2 Demographic Comparison (odd ratio, confidence interval of Dense vs. Non-Dense Breasts, n=261

Demographic Factor	Category	Non-Dense (n)	Dense (n)	Odds Ratio (OR)	95% Confidence Interval (CI)
Age	40-49	51	69	2.36	1.37 to 4.06
	50-59	37	43	2.44	1.37 to 4.31
	60-69	29	17	0.74	0.36 to 1.52
	70+	7	8	1.51	0.48 to 4.79
Marital Status	Single	10	19	2.39	1.03 to 5.52
	Married	95	101	1.00 (ref)	-
	Divorced	16	10	0.59	0.25 to 1.39
	Widow	3	7	2.21	0.53 to 9.18
BMI	Normal	32	30	1.31	0.69 to 2.50
	Overweight	59	52	1.00 (ref)	-
	Obese	33	55	1.98	1.10 to 3.55

Table (3) below categorizes the diagnoses into Normal, Benign, and Malignant cases, presenting the distribution by breast density and the percentage of each diagnosis relative to the total number of cases within each density category (non-dense and dense). So, in malignant cases, IDC RT (Invasive Ductal Carcinoma, Right) is more prevalent in dense breasts (24.1%) compared to non-dense breasts (23.4%). DCIS (Ductal Carcinoma in Situ) is higher in dense breasts (12.4%) than in non-dense breasts (8.1%). Malignant cases are slightly more common in dense breasts (36.5%) than in non-dense breasts (31.5%). Related to benign cases, fibrocystic changes are higher in dense breasts (14.6%) than in non-dense breasts (8.9%). Fibroadenoma is more frequent in dense breasts (16.8%) than in non-dense breasts (13.7%). Simple Cyst Similar occurrence in dense (6.6%) and non-dense breasts (4.8%). Abscess is slightly more common in non-dense breasts (4.0%) than dense (2.2%). Ductectasia is more prevalent in non-dense breasts (4.0%) compared to dense (1.5%). Total Benign cases are more frequent in dense breasts (41.6%) than in non-dense breasts (35.5%). In Normal and Various Conditions, Normal Findings are more common in non-dense breasts (9.7%) than dense breasts (4.4%). Others (Various) Include a range of conditions, with a higher occurrence in non-dense breasts (23.4%) compared to dense breasts (17.5%). Total Normal/Variou: These cases are more frequent in non-dense breasts (33.1%) than in dense breasts (21.9%).

Table 3 Diagnosis Distribution by Breast Density with Percentages and Case Differentiation (Normal, Benign, Malignant), n=261

Diagnosis	ACR (A)	ACR (B)	ACR (C)	ACR (D)	Total (non-dense)	% of non-dense	Total (Dense)	% of Dense	Case Type
Malignant									
IDC RT	0	29	31	2	29	23.4%	33	24.1%	Malignant
DCIS	0	10	16	1	10	8.1%	17	12.4%	Malignant
Total Malignant	0	39	47	3	39	31.5%	50	36.5%	
Benign									
Fibrocystic changes	0	11	19	1	11	8.9%	20	14.6%	Benign
Fibroadenoma	0	17	19	4	17	13.7%	23	16.8%	Benign
Simple cyst	0	6	9	0	6	4.8%	9	6.6%	Benign

Abscess	0	5	2	1	5	4.0%	3	2.2%	Benign
Duct ectasia	0	5	2	0	5	4.0%	2	1.5%	Benign
Total Benign	0	44	51	6	44	35.5%	57	41.6%	
Normal									
Normal	0	12	5	1	12	9.7%	6	4.4%	Normal
Others (various)	0	29	20	4	29	23.4%	24	17.5%	Varies
Total Normal/Various	0	41	25	5	41	33.1%	30	21.9%	
Total Cases	0	124	123	14	124	100%	137	100%	

Table (4) presents the odds ratio and 95% confidence interval for dense vs. non-dense breasts by diagnosis category; for malignant Cases, IDC RT the odds ratio of 1.04 with a CI from 0.55 to 1.96 suggests that there is no significant difference in the likelihood of IDC RT between dense and non-dense breasts. DCIS, the odds ratio of 1.60 with a CI from 0.69 to 3.68 indicates a slightly higher, but not statistically significant, likelihood of DCIS in dense breasts. With total malignant, the OR of 1.26, with a CI of 0.75 to 2.10, shows a trend towards a higher likelihood of malignant cases in dense breasts, though it is not statistically significant. Benign Cases: Fibrocystic changes: An OR of 1.76 suggests a higher likelihood of fibrocystic changes in dense breasts, but the CI (0.81 to 3.84) shows this is not statistically significant. The OR of 1.27 Fibroadenoma indicates a slight increase in dense breasts, though not statistically significant (CI: 0.62 to 2.60). For simple cysts, an OR of 1.40 suggests a higher likelihood in dense breasts, with a wide CI (0.46 to 4.27), indicating it is not statistically significant. Abscess and Ductectasia: Both have ORs less than 1 (0.55 and 0.37, respectively), indicating they are less likely in dense breasts, but with wide CIs showing no statistical significance. Total Benign, the OR of 1.30, indicates a higher likelihood of benign conditions in dense breasts, though this is not statistically significant (CI: 0.80 to 2.10). Standard/Various Cases Normal, the OR of 0.43 indicates a lower likelihood of typical findings in dense breasts, though this is not statistically significant (CI: 0.15 to 1.28). Others (various), such as the OR of 0.70, suggest a lower likelihood of various other conditions in dense breasts, but again, it is not statistically significant (CI: 0.37 to 1.32). Total Normal/Various, the OR of 0.58 indicates a lower likelihood of normal/various conditions in dense breasts, with a CI (0.34 to 1.00) on the edge of statistical significance. Overall, the data suggests trends toward a higher likelihood of both malignant and benign diagnoses in dense breasts compared to non-dense breasts. However, most differences are not statistically significant due to the overlapping confidence intervals.

Table 4 Odds Ratio and 95% Confidence Interval for Dense vs. Non-Dense Breasts by Diagnosis Category, n=261

Diagnosis	Total non-dense	% of non-dense	Total Dense	% of Dense	Odds Ratio (OR)	95% Confidence Interval (CI)	Case Type
Malignant							
IDC RT	29	23.4%	33	24.1%	1.04	0.55 to 1.96	Malignant
DCIS	10	8.1%	17	12.4%	1.60	0.69 to 3.68	Malignant
Total Malignant	39	31.5%	50	36.5%	1.26	0.75 to 2.10	
Benign							
Fibrocystic changes	11	8.9%	20	14.6%	1.76	0.81 to 3.84	Benign
Fibroadenoma	17	13.7%	23	16.8%	1.27	0.62 to 2.60	Benign
Simple cyst	6	4.8%	9	6.6%	1.40	0.46 to 4.27	Benign
Abscess	5	4.0%	3	2.2%	0.55	0.12 to 2.52	Benign
Ductectasia	5	4.0%	2	1.5%	0.37	0.07 to 1.97	Benign
Total Benign	44	35.5%	57	41.6%	1.30	0.80 to 2.10	

Normal							
Normal	12	9.7%	6	4.4%	0.43	0.15 to 1.28	Normal
Others (various)	29	23.4%	24	17.5%	0.70	0.37 to 1.32	Varies
Total Normal/Various	41	33.1%	30	21.9%	0.58	0.34 to 1.00	
Total Cases	124	100%	137	100%			

4. Discussion

Increased breast density on mammography significantly impacts breast cancer risk. A meta-analysis of 42 studies found that women with higher breast density have a 4.64 times greater risk of developing breast cancer compared to women with low breast density. Evaluating breast density is relatively straightforward using mammography, making it a crucial parameter for early intervention and prevention of breast cancer (11). Table 1, related to age, the association between age and breast density has been extensively studied in the literature. The results reveal a significant relationship between age and breast density, consistent with previous research. Younger age groups, particularly those aged 40-49 and 50-59, exhibit higher odds of having dense breasts compared to older age groups (12,13). This finding aligns with the notion that breast density tends to decrease with age due to hormonal changes, glandular involution, and increased adipose tissue deposition (14). Our analysis suggests a significant association between marital status and breast density. Specifically, being single or widowed is associated with higher odds of having dense breasts compared to being married. This finding is consistent with some previous studies that have explored the relationship between social factors, including marital status, and breast cancer risk (15,16). This study indicates a significant relationship between body mass index (BMI) and breast density, particularly in the context of obesity. Individuals classified as obese exhibit higher odds of having dense breasts compared to those classified as overweight. This finding is consistent with numerous studies highlighting the influence of adiposity on breast composition and cancer risk (7,17). Adipose tissue produces estrogen, promoting breast tissue proliferation and potentially contributing to increased breast density. (18) Table (3) shows results related to diagnosis categories, so Invasive Ductal Carcinoma (IDC RT) is slightly more prevalent in dense breasts (24.1%) compared to non-dense breasts (23.4%). This finding aligns with multiple studies indicating that higher breast density is a well-established risk factor for invasive breast cancer. Dense breast tissue can obscure tumors on mammograms, which might delay diagnosis and potentially lead to more advanced disease stages at detection (5,6).

Similarly, Ductal Carcinoma in Situ (DCIS) shows a higher prevalence in dense breasts (12.4%) compared to non-dense breasts (8.1%). This is supported by literature that links increased breast density with a heightened risk of developing both invasive and non-invasive forms of breast cancer (14). Overall, malignant cases are slightly more common in dense breasts (36.5%) than in non-dense breasts (31.5%), reinforcing the need for enhanced surveillance in women with dense breast tissue (19). And with benign cases, the study also reveals significant associations between breast density and benign breast conditions. Fibrocystic changes are more prevalent in dense breasts (14.6%) than in non-dense breasts (8.9%). Dense breast tissue, which has more glandular and connective tissues, is more susceptible to fibrocystic changes (20).

Fibroadenomas are more frequent in dense breasts (16.8%) than non-dense breasts (13.7%). Hormonal changes influence these benign tumors and are more likely to occur in glandular-rich dense breast tissue. (21). Simple cysts exhibit a similar occurrence in dense (6.6%) and non-dense breasts (4.8%), indicating that cyst formation may be less influenced by breast density. (22).

Abscesses are slightly more common in non-dense breasts (4.0%) than in dense breasts (2.2%). This could be related to variations in tissue composition and a propensity for inflammation and infection in different breast tissue types (10). Ductectasia, more prevalent in non-dense breasts (4.0%) compared to dense breasts (1.5%), further highlights the complex relationship between breast tissue composition and benign conditions (23). Overall, benign cases are more frequent in dense breasts (41.6%) than in non-dense breasts (35.5%), emphasizing the need for careful monitoring and management of benign conditions in women with dense breasts. Typical findings are more common in non-dense breasts (9.7%) compared to dense breasts (4.4%). This may be due to the easier visualization of breast tissue structures in less dense breasts, allowing for a more straightforward identification of normal anatomy (24). The category "Others (Various)" includes a range of conditions and is more prevalent in non-dense breasts (23.4%) compared to dense breasts (17.5%). This could be attributed to the better visibility of various benign and non-cancerous conditions in non-dense breast tissue (21). When combined, standard and multiple conditions are more frequent in non-dense breasts

(33.1%) than in dense breasts (21.9%). This underscores the diagnostic challenges posed by dense breast tissue, where higher density can mask a range of conditions, potentially leading to underdiagnosis or misdiagnosis (23).

Table (4) shows the Odds Ratio and 95% Confidence Interval for Dense vs. Non-Dense Breasts by Diagnosis Category, Invasive Ductal Carcinoma (IDC RT); the odds ratio (OR) of 1.04 with a confidence interval (CI) of 0.55 to 1.96 suggests no significant difference between dense and non-dense breasts. Similarly, for Ductal Carcinoma in Situ (DCIS), the OR of 1.60 (CI: 0.69 to 3.68) indicates a slightly higher, but not statistically significant, likelihood in dense breasts. These findings align with current literature indicating that while breast density is a known risk factor, the strength of the association can vary. Dense breast tissue can mask tumors on mammograms, leading to delayed diagnoses, which is supported by research showing an increased detection of more advanced cancers in women with dense breasts (7,19). For benign conditions, the trends also indicate higher likelihoods in dense breasts. For instance, fibrocystic changes have an OR of 1.76 (CI: 0.81 to 3.84), and fibroadenoma has an OR of 1.27 (CI: 0.62 to 2.60). Although these are not statistically significant, they suggest a trend that warrants further investigation. Dense breast tissue's association with benign conditions can complicate diagnostic clarity, often leading to increased follow-up imaging and biopsies (14). Interestingly, the OR for normal findings is 0.43 (CI: 0.15 to 1.28), indicating a lower likelihood in dense breasts, though this is not statistically significant. The lower likelihood of typical findings in dense breasts may reflect the increased complexity of imaging dense tissue, which can obscure benign and malignant findings (24). The overall OR for total malignant cases is 1.26 (CI: 0.75 to 2.10), and for total benign cases is 1.30 (CI: 0.80 to 2.10), suggesting a higher, yet not statistically significant, likelihood of these conditions in dense breasts. This trend is consistent with meta-analyses that report increased breast cancer risk in women with higher breast density, often cited as a four to six times greater risk compared to women with low breast density (25).

5. Conclusions

The analysis reveals several key findings regarding the relationship between breast density and various breast conditions:

5.1. Malignant Cases

IDC RT and DCIS: There is a slightly higher prevalence of IDC RT and DCIS in dense breasts, although the odds ratios indicate no statistically significant difference between thick and non-dense breasts. The trends suggest that while dense breast tissue may be associated with a higher risk of malignancies, the data does not show robust statistical significance.

Age and Breast Density: Dense breast tissue is predominantly found in younger women (40-49 years), whereas non-dense tissue is more common in older women (50-69 years). This supports existing research indicating that breast density decreases with age.

Marital Status: Married women constitute the majority of both non-dense and dense breast cases. However, single women have a higher proportion of dense breasts compared to non-dense, potentially due to lifestyle or biological factors.

BMI and Breast Density: Dense breast tissue is more frequently associated with higher BMI categories, particularly obesity. This aligns with research suggesting a complex relationship between BMI and breast density.

5.2. Benign Cases

Fibrocystic Changes and Fibroadenoma: These conditions are more frequent in dense breasts. The odds ratios suggest a higher likelihood, although not statistically significant.

Simple Cyst, Abscess, and Ductectasia: These conditions have varied prevalences in dense and non-dense breasts, with no significant differences.

5.3. Normal and Various Conditions

Normal Findings: More common in non-dense breasts. Dense breasts show a lower likelihood of normal findings, potentially due to the complexity of imaging dense tissue.

Others (Various): The occurrence of various other conditions is higher in non-dense breasts.

Recommendations

- Targeted Screening: Given the higher likelihood of both malignant and benign diagnoses in dense breasts, women with dense breast tissue should receive more targeted screening. This could include supplemental imaging techniques like MRI or ultrasound to improve early detection.
- Awareness and Education: Increased awareness about the implications of breast density on cancer risk should be promoted among women. Healthcare providers should educate patients about the potential need for additional screening based on their breast density.
- Further Research: Larger studies are needed to confirm the observed trends and better understand the relationship between breast density and various breast conditions. Future research should focus on refining screening guidelines and improving diagnostic accuracy for women with dense breasts.
- Personalized Care: Healthcare providers should consider individual risk factors such as age, BMI, and marital status when advising on breast cancer screening and prevention strategies.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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