



Positive Predictive Value of Malignancy in BI-RADS 4 and 5 Breast Lesions

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Abstract

Objective: To determine the positive predictive value (PPV) of the breast imaging and data system (BI-RADS) category 4 and 5 in diagnosis of breast cancer. The associations of abnormal mammographic findings with BI-RADS 4 and BI-RADS 5 were also determined.

Methods: We identified the list of women who had mammography and ultrasonography in Department of Radiology from January 1st, 2009 to December 31st, 2011. Women who were diagnosed as BI-RAD 4 or BI-RADS 5 and had histopathologic diagnosis were included into the study. Data collected were age, abnormal mammographic and ultrasonographic findings, BI-RADS category and pathological results. The association between each imaging feature, BI-RADS category and pathological results were analyzed.

Results: Total of 7,705 women had mammography in our institution during the study period. Three hundred and two women met inclusion criteria and were included in the study. Mean age was 51.6 ± 11.1 years. BI-RADS 4 diagnosis was made in 74.5% and BI-RADS 5 in 25.5%. Mass was the most common imaging abnormality found in 62.3%. We found that 54.3% of breast lesions was malignant while the other 45.7% was benign. The most common malignant lesion identified in 86.6% was invasive ductal carcinoma. Fibroadenoma and fibrocystic change were the most common benign lesions, found in 20.3% and 18.1% respectively. The positive predictive value of breast cancer in BI-RADS 4 and 5 were 40.4% and 94.8%, respectively.

Conclusion: The BI-RADS categorization is useful in predicting the chance of malignancy. BI-RADS categories 4 and 5 in this study had a probability of malignancy of 40.4% and 94.8%, respectively. Preoperative biopsy should be performed before performing definite treatment in all these lesions.

Key words: mammogram, BI-RADS, malignancy, predictive value



ค่าพยากรณ์บวกของมะเร็งเต้านมในรอยโรคที่จัดอยู่ใน BI-RADS 4 และ 5

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาค่าพยากรณ์บวกของมะเร็งเต้านมในรอยโรคที่ได้รับการวินิจฉัยว่าเข้าได้กับ BI-RADS category 4 และ 5 และศึกษาความผิดปกติทางแมมโมแกรม เปรียบเทียบกับ BI-RADS category 4 และ 5

วิธีดำเนินการวิจัย: ทำการทบทวนผลการตรวจแมมโมแกรมของสตรีที่ได้รับการตรวจที่ภาควิชารังสีวิทยา ตั้งแต่ 1 มกราคม พ.ศ.2552 ถึง 31 ธันวาคม พ.ศ. 2554 คัดเลือกกลุ่มตัวอย่างที่มีรอยโรคที่จัดอยู่ใน BI-RADS 4 และ 5 และมีผลพยาธิวิทยา รวบรวมข้อมูลของอายุ, ผลการตรวจแมมโมแกรม, คลื่นเสียงความถี่สูง, BI-RADS category และผลทางพยาธิวิทยา ทำการเปรียบเทียบความผิดปกติทางรังสี, BI-RADS category และผลทางพยาธิวิทยา

ผลการวิจัย: ในสตรีทั้งหมด 7,705 คน ที่ได้รับการตรวจแมมโมแกรม พบกลุ่มตัวอย่างที่ตรงตามเกณฑ์คัดเข้า 302 ราย อายุเฉลี่ย 51.6 ± 11.1 ปี พบรอยโรคที่จัดอยู่ใน BI-RADS 4 และ BI-RADS 5 ร้อยละ 74.5 และ 25.5 ตามลำดับ ลักษณะภาพทางรังสีที่พบมากที่สุดคือ ก้อน พบร้อยละ 62.3 ผลพยาธิวิทยาเป็นมะเร็งเต้านม ร้อยละ 54.3 ขณะที่กลุ่มที่ไม่ใช่มะเร็งเต้านมพบร้อยละ 45.7 มะเร็งเต้านมชนิดที่พบได้บ่อยที่สุดคือ invasive ductal carcinoma พบร้อยละ 86.6, fibroadenoma และ fibrocystic change พบได้มากที่สุดในกลุ่มที่ไม่ใช่มะเร็งเต้านม ร้อยละ 20.3 และ 18.1 ตามลำดับ ค่าพยากรณ์บวกของมะเร็งเต้านมในรอยโรคที่จัดอยู่ใน BI-RADS 4 และ 5 ร้อยละ 40.4 และ 94.8 ตามลำดับ

สรุป: การรายงานผลแมมโมแกรมแบบ BI-RADS มีประโยชน์ในการพยากรณ์โอกาสที่จะเป็นมะเร็งเต้านมได้อย่างมีประสิทธิภาพ ค่าทำนายผลบวกของมะเร็งเต้านมในรอยโรค BI-RADS 4 และ 5 ในการศึกษาครั้งนี้เท่ากับร้อยละ 40.4 และ 94.8 ตามลำดับ การตรวจชิ้นเนื้อก่อนวางแผนการรักษาจึงมีความสำคัญมาก

Introduction

Breast cancer is the most common cancer in women worldwide.¹ In Thailand, it has surpassed cervical cancer and becomes the most common cancer in Thai women.² Regular breast self-examination, annual physical examination by care provider, and screening mammography can detect early breast cancer.³

Mammography is a simple radiologic tool with high sensitivity for detection of breast lesions. It can be used for either screening in asymptomatic women or performing diagnosis in women with abnormal clinical finding. For screening, the United States Preventive Services Task Force proposed recommendation for women at normal risk for breast cancer that mammography should be done every two years in women between the ages of 50 and 74.⁴ One Cochrane review reported that mammography in women between 50 and 75 years old resulting in a relative risk reduction of death from breast cancer of 15% or an absolute risk reduction of 0.05%.⁵ In contrast, those who have higher risk of breast cancer should have earlier and more frequent test. The example are women who previously had breast cancer, have a strong family history of breast and ovarian cancer, or have BRCA gene mutation. Annual screening mammography is recommended for women with high risk features beginning at age 30 years old.⁶

The benefit of screening mammogram to detect subclinical breast lesion has to be balanced with the side effects from unnecessary surgery in a non-clinical important lesion. Thus, the correlation of mammographic findings with clinical information and final pathologic results should be a major concern for all involved including clinician, radiologist, pathologist and the women themselves.

Many radiologic features are targeted for evaluation in mammography, e.g., character of lesion, density, asymmetry. Several features are described in association with benign or malignant breast lesions; however, some are not specific and cannot definitely discriminate the nature of lesions. The radiologist may be reluctant to give the definite radiologic diagnosis based on only one or

few abnormal features.^{7,8} In order to improve the descriptive diagnosis of each abnormal mammographic feature, in 1992, the American College of Radiology (ACR) first adopted the Breast Imaging Reporting and Data System (BI-RADS) which are recommendation for a clinical care.⁹ The system was revised for a few more times.⁹⁻¹¹ The latest version in 2003¹² has incorporated ultrasonography (US) and/or magnetic resonance imaging (MRI) as an adjunct to mammography especially for those who have abnormal lesion.

Our institution has provided mammography as a part of health program surveillance for healthy women or as a primary diagnostic test to suggest the nature and to delineate the specific site of lesion suspicious from physical examination. It has been nearly 5 years since we had set up the Diagnostic Breast Cancer Center equipped with full-field digital mammographic and ultrasonographic machines. Approximately 2,000 to 2,500 women undergo the surveillance or diagnostic procedure per year. This study aimed to evaluate the positive predictive value (PPV) of mammographic findings categorized as BI-RADS 4 and 5. The association of abnormal mammographic findings with BI-RADS 4 and 5 was also determined.

Methods

The approval from the Ethics Committee of the institution was obtained prior to the study. We identified the list of women who had mammography in our institution between January 2009 and December 2011. Inclusion criteria were women who have either screening mammography without any abnormal clinical findings, or have diagnostic mammography in those with abnormal or suspicious findings from physical examination, and to have BI-RADS 4 or BI-RADS 5. Those who do not have pathologic diagnosis in the institution were excluded.

As a standard procedure, mammography was performed using full-field digital mammographic equipment (Siemens Mammomat Novation DR®, Germany). The practice of the institution generally follows the standard practice. Two standard views

images are obtained (mediolateral oblique and craniocaudal) with additional views as necessary. Supplementary ultrasonography using 5-14 MHz linear array transducers (G E logiq 9®, WI, USA) was performed in almost all patients except women whose breasts are nearly or entirely composed of fatty tissue. Mammographic and sonographic studies were interpreted by one of the radiologists of the institution according to the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS).¹² One of the BI-RADS category along with its recommendation was given according to the most abnormal features from mammography combined with those from ultrasonography as follows:

Category 0: incomplete assessment, additional imaging and/or prior mammograms for comparison are needed.

Category 1: negative study, routine follow-up is recommended.

Category 2: benign findings, routine follow-up is recommended.

Category 3: probably benign lesion, short interval follow-up is recommended.

Category 4: suspicious abnormality, biopsy should be considered.

Category 5: highly suggestive of malignancy, appropriate action should be taken.

Category 6: known biopsy-proven malignancy, appropriate action should be taken.

Women who had BI-RADS 4 or BI-RADS 5 were generally subjected to further clinical investigation. The most common next step of management was fine needle aspiration (FNA) or core needle biopsy (CNB). For premalignant or malignant diagnosis, various types of surgical procedures were performed at the discretion of the surgeon.

Data collected were age, symmetry and side of lesion, skin integrity, any abnormal features of mass, microcalcifications, axillary lymphadenopathy, architectural distortion, sign of inflammation, BI-RADS category, and histopathologic diagnosis. The most important or most severe pathologic diagnosis was taken for the analysis. Data were

analyzed using SPSS statistical software, version 11.5. Continuous data was represented as mean with standard deviation or median with range. Categorical data was presented as number and percentage. Association between BI-RADS category and the status of malignancy were compared using chi-squared or Fisher's exact test.

Results

We identified 7,705 women who underwent mammography and ultrasonography during the study period in our institution. BI-RADS category of all 7,705 women is shown in Table 1. There were 441 women (5.7%) categorized as BI-RADS category 4 and 5. No pathologic diagnosis was available in 139 women, thus they were excluded from our study. Mean age of 302 women who were included in our study was 51.6 ± 11.1 years (range 17-83 years). BI-RADS 4 was diagnosed in 225 women (74.5%) and BI-RADS 5 in 77 women (25.5%). We found an approximately equal chance of having abnormal breast image from each unilateral sides, i.e., 47.9% right and 49.5% left, while 2.6% were bilateral.

Among abnormal imaging features, the most common finding was mass lesion that was found in 188 breast images (62.3%). Microcalcifications were found in 22 breasts (7.2%). Seventy nine breast images (26.2%) had combined features of mass and microcalcifications. Sign of inflammation was found in only two breast images (0.7%). Details of abnormal imaging features according to the BI-RADS category are shown in Table 2.

Primary investigation for breast lesions in our institution was either FNA or CNB. Those who had premalignant/malignant diagnosis underwent definite surgical procedure. Final pathologic diagnosis was obtained from surgical excision of the lesion in 155 women (51.3%). Of 302 total women, 164 specimens (54.3%) were malignant while 138 (45.7%) were benign. Detail of pathologic diagnosis of benign and malignant breast lesions according to their BI-RADS category are shown in Table 3 and 4, respectively. Invasive ductal carcinoma was the most frequent malignant lesion

Table 1:

BI-RADS category in all women having mammography and ultrasonography between 2009-2011 (N=7,705)

BIRADS classification	N	%
B1	2,425	31.5
B2	3,335	43.3
B3	1,479	19.2
B4	346	4.5
B5	95	1.2
B6	25	0.3
Total	7,705	100.0

Table 2:

Abnormal imaging features according to the BI-RADS category (N=302)

Abnormal mammographic features*	BI-RADS category		N (%**)
	BI-RADS 4 n=225 (%)	BI-RADS 5 n=77 (%)	
Mass	150 (79.8)	38 (20.2)	188 (62.3)
Microcalcifications	22 (100.0)	0 (0.0)	22 (7.2)
Mass with microcalcifications	39 (49.4)	40 (50.6)	79 (26.2)
Axillary lymphadenopathy	18 (43.9)	23 (56.1)	41 (13.6)
Architectural distortion	21 (63.6)	12 (36.4)	33 (10.9)
Skin involvement	10 (41.7)	14 (58.3)	24 (7.9)
Asymmetrical density	20 (83.3)	4 (16.7)	24 (7.9)
Inflammatory reaction	2 (100.0)	0	2 (0.7)

* Note: One subject may have more than 1 abnormal imaging feature.

** Percentage of abnormal imaging features was obtained from total of 302 women

found in our series, 142 cases (86.6%), while fibroadenoma, 28 cases (20.3%), and fibrocystic lesions, 25 cases (18.1%) were the two most common benign lesions found. Examples of imaging features of invasive ductal carcinoma and fibroadenoma are shown in Figure 1 and 2, respectively.

We studied the association between BI-RADS category and malignancy. We found that BI-RADS category 5 showed significant associations with premalignant or malignant findings compared to BI-RADS category 4 ($P < 0.001$). In summary, 91 of

the 225 women with BI-RADS 4 turned out to be malignant while 73 out of 77 BI-RADS 5 were malignant (Table 5). The positive predictive values of BI-RADS categories 4 and 5 were 40.4% and 94.8% respectively.

Discussion

There are several mammographic and ultrasonographic features that can be used to differentiate between benign and malignant breast lesions. These features are primary signs, e.g., shape of the lesion, margin, density, and

Table 3:

Benign pathologic diagnosis of breast lesions according to the BI-RADS category (N=138)

Benign pathologic diagnosis	BI-RAD category		Total N (%*)
	BI-RADS 4 n = 134 (%)	BI-RADS 5 n = 4 (%)	
Fibroadenoma	28 (100.0)	-	28 (20.3)
Fibrocystic change	25 (100.0)	-	25 (18.1)
Papilloma	10 (100.0)	-	10 (7.2)
Sclerosing adenosis	3 (100.0)	-	3 (2.2)
Chronic inflammation	18 (90.0)	2 (10.0)	20 (14.5)
Phyllodes tumor	14 (93.3)	1 (6.7)	15 (10.9)
Focal adenosis	2 (100.0)	-	2 (1.4)
Cystic lymphangioma	1 (100.0)	-	1 (0.7)
Lobular hyperplasia	1 (100.0)	-	1 (0.7)
Reactive lymphoid hyperplasia	2 (100.0)	-	2 (1.4)
Ductal hyperplasia	1 (100.0)	-	1 (0.7)
Benign breast tissue	27 (96.4)	1 (3.6)	28 (20.3)
Granulation tissue	1 (100.0)	-	1 (0.7)
Fat necrosis	1 (100.0)	-	1 (0.7)
Total	134 (100.0)	4 (100.0)	138 (100)

* Percentage was obtained from each benign diagnosis from total of 138 benign lesions

Table 4:

Malignant pathologic diagnosis of breast lesions according to the BI-RADS category (N=164)

Malignant pathologic diagnosis	BI-RADS category		Total %
	BI-RADS 4	BI-RADS 5	
Invasive ductal carcinoma	79(55.6)	63(44.4)	142(86.6)
Ductal carcinoma in situ	6(75.0)	2(25.0)	8(4.9)
Invasive lobular carcinoma	2(25.0)	6(75.0)	8(4.9)
Metastatic carcinoma to axillary lymph node	4(80.0)	1(20.0)	5(3.0)
Metaplastic carcinoma	-	1(100)	1(0.6)
Total	91(100)	73(100)	164(100)

calcification.^{13,14} Features suggesting malignancy are irregular shape, indistinct, ill-defined or speculated margin, high density mass and fine, linear or fine-linear branching calcifications and

pleomorphic calcifications.^{13,14} These features require additional investigation to verify nature of the mass. The associated findings which will also suggest malignancy are skin retraction, nipple

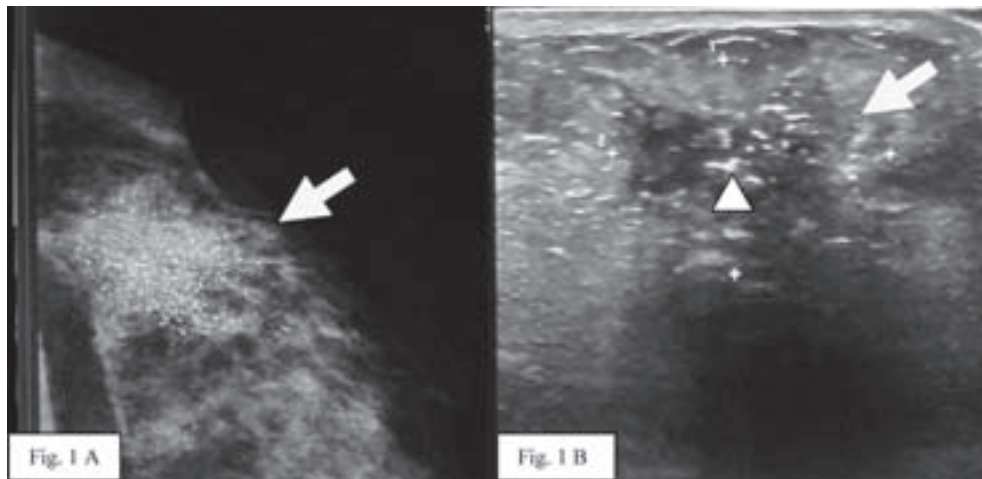


Figure 1: A 50 years old woman presented with a palpable left breast mass. Mammogram (Figure 1A) revealed a spiculated lesion with pleomorphic calcifications (arrow). Ultrasonogram (Figure 1B) demonstrated an irregular solid mass with indistinct border (arrow) and calcifications (arrowhead). BI-RADS 5 diagnosis was given. Pathologic diagnosis was invasive ductal carcinoma.

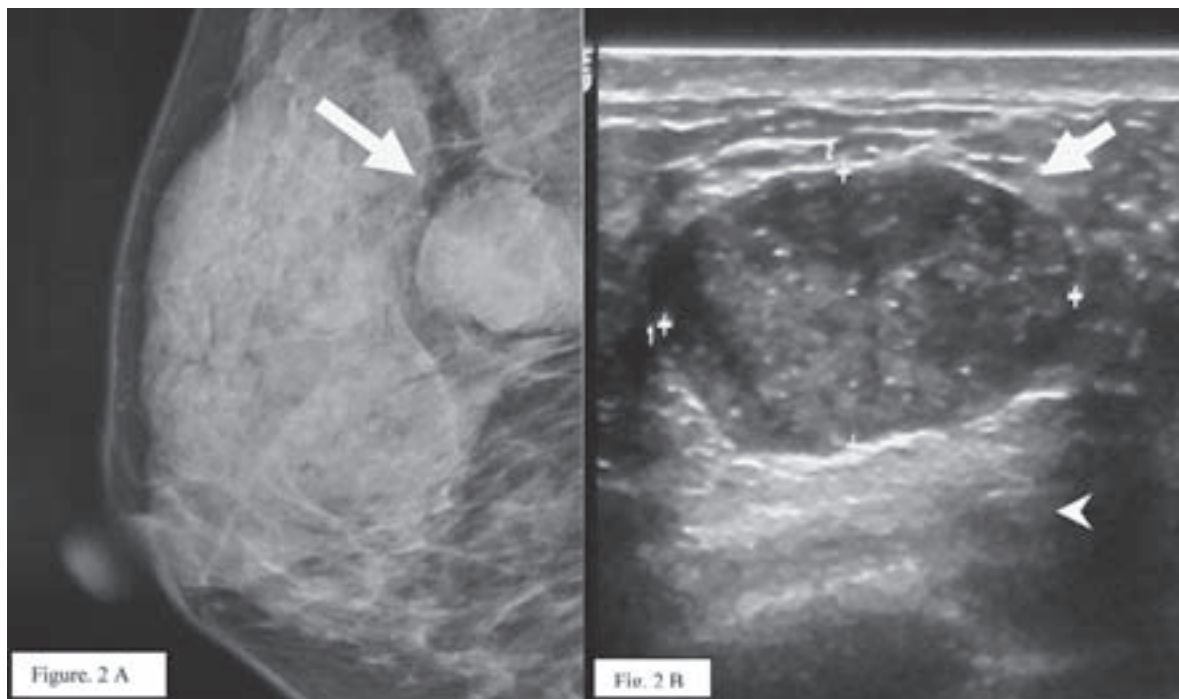


Figure 2: A 48 years old woman presented with a palpable right breast mass. Mammogram (Figure 2A) shows a macrolobulated mass at upper outer quadrant (arrow). Ultrasonogram (Figure 2B) demonstrated thin encapsulated mass (arrow) with area of posterior enhancement (arrowhead). BI-RADS 4 diagnosis was made. Pathologic diagnosis was fibroadenoma.

Table 5:

BI-RADS category according to the status of malignancy of breast lesions (N=302)

BI-RADS	Status of breast lesions		Total
	Benign	Malignant	
4	134 (59.6)	91 (40.4)	225 (74.5)
5	4 (5.2)	73 (94.8)	77 (25.5)
Total	138 (45.7)	164 (54.3)	302 (100)

retraction, skin thickening, coarse trabeculation, axillary adenopathy, architectural distortion and asymmetrical density.^{13,14} Skin thickening and coarse trabeculation represent swelling of breast tissue.

Although it can be caused by other inflammatory lesions, axillary adenopathy in the context of breast mass generally represents axillary lymph node metastasis. Architectural distortion represents retraction of tumor cells.¹⁴ Architectural distortion and asymmetrical density must be differentiated from scar from previous surgery. Asymmetric breast tissue is another helpful feature yet quite difficult for an evaluation. Normal breasts may have slight asymmetry while prominent asymmetry is suggestive of malignant lesion, especially when associated with architectural distortion or calcifications. In the evaluation of masses, the final assessment is often determined by a combination of the mammographic, ultrasonographic and clinical findings.^{13,15} With several abnormal findings, biopsy should be considered.

Mass was the most common abnormal radiographic imaging in our study, 62.3%. Other studies of Wiratkapun et al¹⁶ and Muttarak et al¹⁷ also reported mass as the most common finding identified in 48.5% and 56.7% respectively. We found microcalcifications in 7.2% which was also in the range of 6-7% as previously reported.^{16,17} Mass with microcalcifications was identified in 26.2% which is similar to 21.5% in Muttarak’s study¹⁷ yet lower than that found in the study of Wiratkapun et al.¹⁶ which was as high as 39.2%. The differences may be explained by the inclusion criteria in the

Wiratkapun study which included only breast lesions with BI-RADS 5, which generally have more frequent findings of both mass and microcalcifications features.¹⁶ Regarding benign lesions, fibroadenoma and fibrocystic change were the two most common lesions found in our study as well as previous studies.^{16,17}

BI-RADS system is an objective assessment taking all mammographic features into account. The diagnostic performances of using BI-RADS system to detect malignancy are high with PPV of BI-RADS 4 and 5 ranging from 23-34% and 81-97% respectively.¹⁸⁻²¹ Our study found PPV of 40.4% and 94.8% in BI-RADS 4 and 5 which were in the ranges previously reported.¹⁸⁻²¹

The results of invasive ductal carcinoma was high in this study (86.6%) which is not significantly different from 89.5% from Wiratkapun’s¹⁶ and 79.2% from Muttarak’s study.¹⁷ This is because all the studies focused only on BI-RADS 4 and 5. Although BI-RADS category 5 lesions have a high probability of being cancerous, false positive or negative may be possible. Preoperative histologic diagnosis particularly by percutaneous core needle biopsy should be performed before definitive surgery.¹² Our study found that 4 women (5.2%) were presented with BI-RADS category 5 and were later found on subsequent biopsy to have benign pathology. Three of them had ill-defined hypoechoic masses with asymmetrical density which were revealed to be only chronic mastitis or granulation tissue. Imaging features of one of these cases are shown in Figure 3. This false positive finding was also recognized in other reports that an ill-defined mass with spiculation, increased density

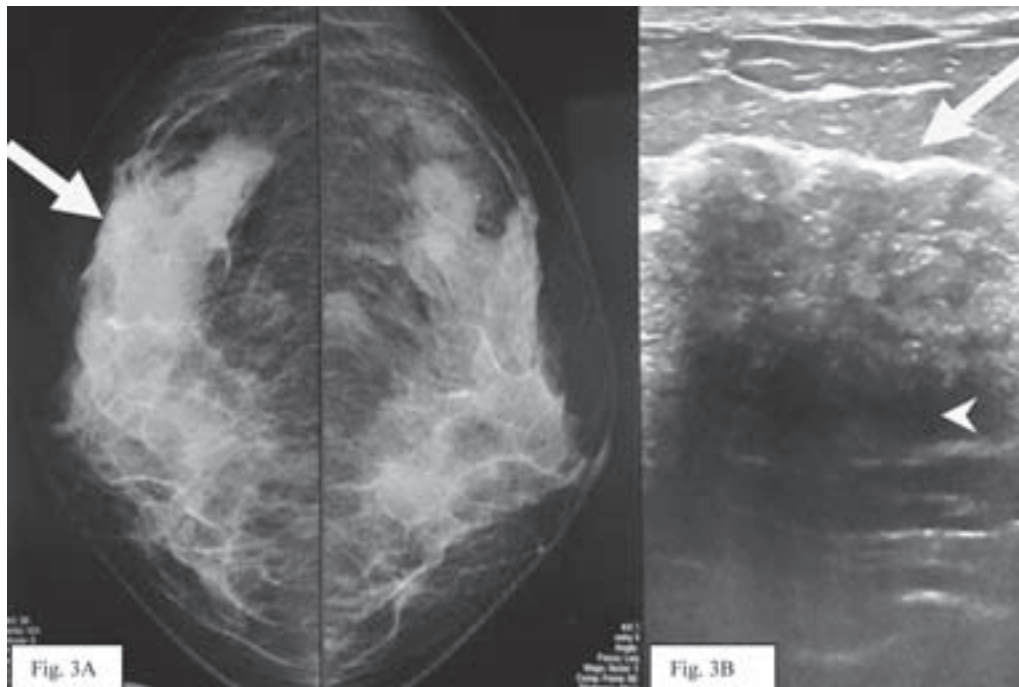


Figure 3: A 53 years old woman with diabetes mellitus presented with a palpable right breast mass with mammographic and ultrasonographic features mimicking malignancy. Mammogram (Figure 3A) showed asymmetrical breast tissue with dense area over mid-lateral region of right breast (arrow). Ultrasonogram (Figure 3B) demonstrated ill-defined hypoechoic mass-like appearance (arrow) with strong posterior shadowing (arrow head). Malignancy was suspected with the diagnosis of BI-RADS 5. Pathology turned out to be chronic mastitis, compatible with diabetic fibrous mastopathy.

and/or complex mass, or architectural distortion could be found in breast infection or tissue reaction from previous surgery.^{13,14} These mammographic and ultrasonographic features may mimic malignancy.^{13,14} The last false positive case had lobulated hyperdense mass with pleomorphic calcifications, so this was diagnosed as BI-RADS category 5. Its histopathology turned out to be benign cystosarcoma phylloides. The phylloides tumors may have large lobulated mass with homogeneous or heterogeneous echogenicity which was difficult to differentiate benign or malignant from mammogram or ultrasonogram.²²

The strong point of this work is that we had pathologic results in nearly all women with BI-RADS 4 and 5. Besides, the final pathologic diagnoses were obtained from surgical excision of the lesions in high percentages (51.3%) of these

women. This surgical excision procedure was theoretically considered to yield better result than the fine needle aspiration. Nevertheless, we were aware of some limitations of our study. These included small number of subjects who had BI-RADS 4- BI-RADS 5, and a lack of follow-up data for those with BI-RADS 1-3. Furthermore, only one radiologist interpreted the mammographic findings, so the results might be subjected to personal experience and attitude to make a definite diagnosis of BI-RADS 4-5.

We hope that our data will serve as a database for radiologists as well clinicians in our institution to be aware of the association between mammographic diagnosis and final pathologic results. Further study should include a larger number of women with and without mammographic abnormalities. A prospective study

is probably required that the radiologists have an agreement the extent and detail of abnormalities before making their mammographic diagnosis. Lastly, inter- and intra-observer variability should be addressed to reduce a subjective interpretation.

Conclusion

BI-RADS categorization is very useful in predicting malignant breast lesion. BI-RADS categories 4 and 5 in this study had a malignant probability of 40.4% and 94.8% respectively. BI-RADS category 5 lesions in patients with palpable breast mass with or without calcifications has very high risk of malignancy. Any single abnormal feature should be considered for further investigations for there are certain risks of malignancy. Both clinicians and radiologists should discuss for an optimal investigation and management to obtain the best outcome.

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