

Original Research Article

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Accuracy of mammography and sonomammography and its correlation with histopathology in the detection of breast cancer

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ABSTRACT

Background: Mammography (MMG) plays a pivotal role in the early diagnosis of breast cancer (BC). However, it is sometimes difficult to use it to diagnose palpable breast lesions among young patients. Ultrasound can be used as an adjunct in differentiating cystic and solid masses. Studies evaluating the combination of MMG and sonomammography (SMG) as an adjunct to detect Breast cancer, are quite scarce in the literature. This study aimed to assess the accuracy of MMG and to comprehend the role of ultrasound as an adjunct to MMG for finding breast lesions.

Methods: Women attending the outpatient department (OPD) with complaints of breast lump, or those undergoing MMG screening were included. All patients then subsequently underwent MMG, SMG and biopsy. MMG and SMG findings were then correlated with the histopathology results.

Results: Irregular shape and calcifications (MMG) and hypoechoic pattern (SMG) were found to be significant features differentiating malignant from benign lesions. Calcifications in benign tumors were observed 5.05 times less frequently than in malignant tumors. MMG combined with SMG had a sensitivity of 90.4%, specificity of 82.4%, positive and negative predictive value of 95% and 67% respectively, along with an accuracy of 88.9% in differentiating benign from malignant masses.

Conclusions: SMG used as an adjunct to MMG is a reliable modality, especially in detecting lesions that are not picked up on MMG, including intraductal papilloma and duct ectasia.

Keywords: Diagnostic imaging, Ultrasonography, Pathology, Breast neoplasms

INTRODUCTION

Breast cancer (BC) in India ranks second in cancers among females, with an age-adjusted incidence and mortality rate of nearly 25.8 and 12.7 per 100,000 individuals, respectively.¹ Among its patients, the most common complaint is the occurrence of breast lump, which has a relatively high prognostic value for malignancy.² Delayed disease presentation can be due to lack of awareness, illiteracy or financial constraints and results in late diagnosis. Early screening and diagnosis of BC are vital as it decreases the BC mortality rate and hikes the rate of

successful outcomes with comprehensive medical treatment.³

Clinical examination, mammography (MMG), ultrasonography (USG), magnetic resonance imaging (MRI), dedicated nuclear isotope scans and biopsy are the various detection and screening methods of BC. However, MMG is considered the gold-standard screening modality in the detection of BC, especially among patients with non-palpable carcinoma.⁴ USG, MRI and molecular breast imaging are usually not considered as primary screening tools and are employed as adjuncts to assess the abnormalities detected in MMG.⁵ American college of

radiography developed the breast-imaging reporting and data system (BI-RADS) lexicon, a standard terminology used to summarize the findings of various breast-imaging techniques such as MMG, USG and MRI.⁴ We too employed the BI-RADS lexicon in our study.

Although MMG plays a central role in BC diagnosis, it is difficult to use it to diagnose palpable breast lesions in young patients, who are susceptible to radiation damage, due to a low positive predictive value and limited sensitivity in dense breast tissue.⁶ Therefore, USG can be used as an adjunct in differentiating cystic and solid masses.⁷ Studies have also stated that the combination of sonomammography (SMG) with MMG reduces the mortality rate by 22% in females 50 years and above, and by 15% in women between 40-49 years.^{8,9} Therefore, in our study, we used both the imaging modalities together to increase the sensitivity and specificity for detecting breast lesions. The present study aimed to assess the accuracy of MMG and to comprehend the role of ultrasound as an adjunct to MMG for detecting breast lesions.

METHODS

A prospective cross-sectional study was conducted at the department of general surgery for two years, from November 2016 to November 2018, in a tertiary hospital in Bangalore, India. Women attending the OPD with complaints of a lump in the breast, or those who elected to undergo MMG screening were included in this study. A total of 90 patients were recruited using a convenience sampling technique for this study. Written informed consent was taken from the selected patients before study initiation. Ethical clearance was also sought from the institutional ethical committee before the initiation of the study. Asymptomatic women, along with women having a lump in the breast, undergoing MMG and SMG with subsequent biopsies (histopathological examinations) were included in the study. Pregnant or lactating women, and women who were previously diagnosed with breast carcinoma or who underwent only fine needle aspiration cytology (FNAC) after MMG were excluded from this study.

Data collection

A structured pre-prepared case proforma was used to record the demographic data. A detailed clinical history containing history of menstrual cycle, mastalgia or lactation, previous family history of any breast problems were recorded, along with the findings of physical examination of those patients who met the inclusion criteria.

Mammography

Lilyum, BET Medical Ltd [India] MMG unit was used for breast MMG using standard views i.e. medio-lateral, oblique and crano-caudal views. The features of MMG were then used to characterize the mass/lesion as benign or

malignant, considering the mass shape (oval, round or irregular), margin (circumscribed, microlobulated, spiculated or ill-defined), calcification (punctuate, coarse, micro or granular), architectural distortion and nipple retraction.

Sonomammography

Voluson Pro 730, GE Healthcare [India] ultrasound unit was used for breast's USG examination. The characteristics of SMG were used to categorize lesions into benign or malignant, based on gray-scale findings, such as mass shape (oval, round or irregular), margin (circumscribed, microlobulated or spiculated), orientation (parallel or non-parallel), posterior acoustic shadow (no features, enhancement, shadowing or combined), lesion boundary (abrupt interface or echogenic halo) and echo pattern (hyperechoic, isoechoic, hypoechoic, complex or anechoic).

All findings were read and interpreted by well-trained radiologists. A final assessment was later made according to BIRADS lexicon score. The lesions were classified as benign, malignant, probably benign or probably malignant.

Histopathological examination

The MMG and SMG results were correlated with histopathology results for the lesion to be finally considered malignant or benign. Histopathology was performed in the form of trucut or excision biopsy. Non-diagnostic smears were repeated several times to improve the accuracy of the findings.

Statistical analysis

Based on previous study, the accuracy of MMG was noted to be 75%.¹² Therefore, the sample size was calculated considering relative precision of 12% and the alpha error of 5%, yielding a sample size of 89 patients. Hence, a total of 90 patients were included in the study.

Statistical package for the social sciences (SPSS) v 18.0 and R environment v 3.2.2 were used for data analysis. Descriptive statistics for detecting breast lesions using MMG and SMG of the breast were calculated and presented as frequency and percentages. The accuracy of MMG in comparison to histopathology and SMG was calculated. The sensitivity, specificity, positive and negative predictive values of MMG and SMG were evaluated to detect breast lesions based on the breast's MMG and SMG results. Mc Nemars test was used to compare the sensitivity and specificity of MMG and SMG of the breast in the evaluation of breast lesions.

RESULTS

Of the 90 patients who presented with a breast lump, most belonged to the age group of 41-60 years. Clinical

characteristics of patients are presented in Table 1. Majority of the patients had a lump in the right side of the breast, no nipple discharge and no family history of BC. Out of 18 women who had mastalgia, 16 had breast malignancy, one had nonspecific breast abscess with duct ectasia and another patient had ductal papilloma. Out of nine patients with nipple discharge, five were associated with carcinoma breast, three with duct papilloma and one with duct ectasia.

Table 1: Clinical characteristics of the study patients.

Characteristics	Number of patients, n=90 (%)
Lump in the breast	
Left	42 (46.7)
Right	48 (53.3)
Mastalgia	
No	72 (80)
Yes	18 (20)
Nipple retraction/discharge	
No	76 (84.4)
Discharge	9 (10)
Retraction	5 (5.6)
Positive family history	
No	81 (90)
Yes	8 (8.9)
Ovarian cancer	1 (1.1)

Following histopathological examination, 17 showed benign lesions while 73 showed malignant lesions, with infiltrating ductal carcinoma (68.9%) being the predominant type of BC (Table 2).

A significant number of malignant masses had irregular shape and calcifications with p value of 0.037, as presented in Table 3. Majority of malignant masses had a well-defined margin; however, this feature was found to be

insignificant. Architectural distortion was noted in only 15% of malignant cases and was statistically insignificant.

On SMG evaluation, the most common shape for malignant masses was lobulated, with a well-defined margin. However, both these criteria were found to be insignificant. Echo pattern was found to be a significant characteristic, with most of the malignant masses having a hypoechoic pattern (63%; p=0.007), as shown in Table 4. Most malignant cases had vascularity (mild or extensive), however, this was statistically insignificant.

Out of the eight features from MMG (mass shape, margin, architectural distortion, calcifications) and SMG (shape, margin, echo pattern, vascularity), the MMG feature of calcification was found to be the most significant – to differentiate a malignant tumor from benign. It was also found that the calcification observed in benign tumors was 5.05 times lesser when compared to that in malignant tumors. A tumor devoid of calcification is a potential sign of benignity (Table 5).

BIRADS score of patients in relation to histopathological findings are given in Table 6. One case of BIRADS 2 was noted to be malignant (infiltrating ductal carcinoma) and six cases of BIRADS 3 were found to be malignant, on histopathological examination. Most of BIRADS 4 cases turned out to be malignant.

There was one case reported as BIRADS 4C that had a benign condition (duct papilloma with fibrocystic changes). All these cases had features of microcalcifications, spiculated margins and the presence of vascularity on MMG and SMG. All the cases reported as BIRADS 5 and 6 were malignant.

Out of 90 cases, 66 were true positive and 14 were true negative. Of the remaining 10 cases who had BIRADS 3 (possibly a benign disease), four were noted to be benign and six were found malignant (Table 7).

Table 2: Histopathological findings of breast cancer patients.

Histopathology	Number of patients, n=90
Infiltrating ductal carcinoma	62 (68.9)
Invasive lobular carcinoma	6 (6.7)
Fibroadenoma	5 (5.6)
Mucinous carcinoma	4 (4.4)
Duct papilloma with fibrocystic changes with epithelial hyperplasia	3 (3.3)
Benign lesion	2 (2.2)
Nonspecific abscess with duct ectasia	2 (2.2)
Benign phyllodes tumor	1 (1.1)
Focal Ductal carcinoma in situ	1 (1.1)
High grade ductal carcinoma in situ	1 (1.1)
Multiple papillomas with florid adenosis and fibrocystic changes	1 (1.1)
Chronic mastitis	1 (1.1)
Fibrocystic changes	1 (1.1)

Table 3: Mammography findings of patients in relation to histopathology.

Mammography	Histopathology		Total (n=90)	P value
	Benign (n=17) %	Malignant (n=73) %		
Mass shape				
Not commented	12 (70.6)	31 (42.5)	43 (47.8)	
Commented	5 (29.4)	42 (57.5)	47 (52.2)	
Irregular	2 (11.8)	30 (41.1)	32 (35.6)	
Oval	2 (11.8)	6 (8.2)	8 (8.9)	0.037*
Lobulated	1 (5.9)	2 (2.7)	3 (3.3)	
Round	0 (0)	2 (2.7)	2 (2.2)	
Ill-defined	0 (0)	1 (1.4)	1 (1.1)	
Well-defined	0 (0)	1 (1.4)	1 (1.1)	
Margin				
Not commented	6 (35.3)	20 (27.4)	26 (28.9)	
Commented	11 (64.7)	53 (72.6)	64 (71.1)	
Well-defined	8 (47.1)	20 (27.4)	28 (31.1)	0.518
Ill-defined	1 (5.9)	19 (26)	20 (22.2)	
Spiculated	2 (11.8)	14 (19.2)	16 (17.8)	
Architectural distortion				
No	15 (88.2)	62 (84.9)	77 (85.6)	1.000
Present	2 (11.8)	11 (15.1)	13 (14.4)	
Calcifications				
No	13 (76.5)	29 (39.7)	42 (46.7)	0.00**
Yes	4 (23.5)	44 (60.3)	48 (53.3)	
Other features				
Axillary lymph nodes	0 (0)	11 (15.1)	11 (12.2)	
Skin thickening	1 (5.9)	4 (5.5)	5 (5.6)	
Asymmetry	2 (11.8)	2 (2.7)	4 (4.4)	
B/l axillary lymph nodes	1 (5.9)	2 (2.7)	3 (3.3)	
Nipple retraction	0 (0)	2 (2.7)	2 (2.2)	
Adjacent skin thickening	0 (0)	1 (1.4)	1 (1.1)	
Retraction of nipple skin thick	0 (0)	1 (1.4)	1 (1.1)	
Right axillary LN	0 (0)	1 (1.4)	1 (1.1)	
Septations	0 (0)	1 (1.4)	1 (1.1)	

*Significant, **highly significant

Table 4: Sonomammography findings of patients in relation to histopathology.

Sonomammogram	Histopathology		Total (n=90)	P value
	Benign (n=17)	Malignant (n=73)		
Shape				
Not commented	8 (47.1)	24 (32.9)	32 (35.6)	
Commented	9 (52.9)	49 (67.1)	58 (64.4)	
Lobulated	5 (29.4)	20 (27.4)	25 (27.8)	
Irregular	3 (17.6)	10 (13.7)	13 (14.4)	
Oval	1 (5.9)	5 (6.8)	6 (6.7)	0.271
Microlobulated	0 (0)	6 (8.2)	6 (6.7)	
Macrolobulated	0 (0)	5 (6.8)	5 (5.6)	
Round	0 (0)	2 (2.7)	2 (2.2)	
Well defined	0 (0)	1 (1.4)	1 (1.1)	
Margin				
Not commented	7 (41.2)	21 (28.8)	28 (31.1)	
Commented	10 (58.8)	52 (71.2)	62 (68.9)	
Well defined	5 (29.4)	19 (26)	24 (26.7)	0.320
Ill defined	3 (17.6)	12 (16.4)	15 (16.7)	
Spiculated	1 (5.9)	4 (5.5)	5 (5.6)	

Continued.

Sonomammogram	Histopathology		Total (n=90)	P value
	Benign (n=17)	Malignant (n=73)		
Irregular	1 (5.9)	15 (20.5)	16 (17.8)	
Macrolobulated	0 (0)	2 (2.7)	2 (2.2)	
Echo pattern				
Not commented	3 (17.6)	7 (9.6)	10 (11.1)	
Commented	14 (82.4)	66 (90.4)	80 (88.9)	
Hypoechoic	9 (52.9)	46 (63)	55 (61.1)	
Heterogeneous	4 (23.5)	17 (23.3)	21 (23.3)	0.007**
Isodense	1 (5.9)	1 (1.4)	2 (2.2)	
Anechoic	0 (0)	1 (1.4)	1 (1.1)	
Mixed echoic	0 (0)	1 (1.4)	1 (1.1)	
Vascularity				
Not commented	10 (58.8)	31 (42.5)	41 (45.6)	
Commented	7 (41.2)	42 (57.5)	49 (54.4)	
Mild	0 (0)	1 (1.4)	1 (1.1)	0.223
Minimal	5 (29.4)	20 (27.4)	25 (27.8)	
Extensive	2 (11.8)	21 (28.8)	23 (25.6)	
Other features				
NA	8 (47.1)	41 (56.2)	49 (54.4)	
Micro calcification	1 (5.9)	7 (9.6)	8 (8.9)	
Dilated duct	5 (29.4)	0 (0)	5 (5.6)	
Axillary lymph nodes	0 (0)	4 (5.5)	4 (4.4)	
Solid and cystic	1 (5.9)	2 (2.7)	3 (3.3)	
B/I small lymph nodes	1 (5.9)	1 (1.4)	2 (2.2)	
Macrocalcifications	0 (0)	2 (2.7)	2 (2.2)	
Punctate microcalcifications	0 (0)	2 (2.7)	2 (2.2)	
Cluster of microcalcifications	0 (0)	2 (2.7)	2 (2.2)	
Lymph nodes	0 (0)	2 (2.7)	2 (2.2)	
Taller than wider	0 (0)	2 (2.7)	2 (2.2)	
Wider than taller	1 (5.9)	1 (1.4)	2 (2.2)	
Areas of necrosis	0 (0)	1 (1.4)	1 (1.1)	
Cystic necrotic areas within the lesion	0 (0)	1 (1.4)	1 (1.1)	
Few calcific foci	0 (0)	1 (1.4)	1 (1.1)	
Left axillary lymph node	0 (0)	1 (1.4)	1 (1.1)	
Microcalcific specks	0 (0)	1 (1.4)	1 (1.1)	
Multiple dilated ducts	0 (0)	1 (1.4)	1 (1.1)	
Specks of calcifications	0 (0)	1 (1.4)	1 (1.1)	

**Highly significant

Table 5: Efficacy of calcification in differentiating malignant and benign lesions.

Tumor type	Calcification		P value	Odds ratio (95% CI)
	Macro and micro calcifications	No calcification		
Benign	4	13	0.01*	5.05 (1.49-17.13)
Malignant	42	27		

*Significant

Table 6: BIRADS score of patients in relation to histopathological findings.

BIRAD score	Histopathology		Total
	Benign (n=17) %	Malignant (n=73) %	
1	1 (5.9)	0 (0)	1 (1.1)
2	4 (23.5)	1 (1.4)	5 (5.6)
3	9 (52.9)	6 (8.2)	15 (16.7)
4	0 (0)	4 (5.5)	4 (4.4)

Continued.

BIRAD score	Histopathology		Total
	Benign (n=17) %	Malignant (n=73) %	
4A	1 (5.9)	18 (24.7)	20 (22.2)
4B	1 (5.9)	17 (23.3)	18 (20.0)
4C	1 (5.9)	15 (20.5)	16 (17.8)
5	0 (0)	9 (12.3)	9 (10)
6	0 (0)	3 (4.1)	3 (3.3)

Table 7: Correlation of BIRADS score with histopathology findings of patients.

Malignant	Observation, n=90				Correlation					Accuracy	P value
	TP	FP	FN	TN	Se	Sp	PPV	NPV			
BIRADS score	66	4	6	14	90.4	82.4	95.7	66.7	88.9	<0.001**	

BIRADS: breast imaging-reporting and data system; TP: true positive; FP: false positive, FN: false negative; TN: true negative; Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value

DISCUSSION

In the present study, BC was detected using MMG along with SMG as an adjunct, and a final assessment was made based on the BIRADS score. BIRADS score was then correlated with histopathological findings for maximizing the accuracy of MMG and SMG findings, and minimizing the variability and false-positive findings. Several studies have also reported that USG in adjunct to MMG increased the cancer detection rate in dense breasts and also minimized the missing diagnoses rate of BC.¹⁰⁻¹³

Breast lump is considered as a predominant sign of malignancy. Hence, patients who attend tertiary care hospitals with complaints of breast lump are quite high.¹⁴ Several studies have also reported that a breast lump is a common complaint among patients attending to breast clinics, which was comparable to our study.^{15,16} It has been reported that knowledge of family history of BC aids in easier identification of breast lesions.¹⁷ However, in our study, most patients had a negative family history for BC.

Infiltrating ductal carcinoma was the most frequent type of BC found in our study, which is quite in line with studies conducted in different regions in other countries.^{18,19} MMG confirms malignant lesion based on the shape, size, margins of lump and number and distribution of calcification. In our study, we confirmed malignant cases through irregular shape and well-defined margins of the lesions. The SMG findings—hypoechoic mass with irregular margin, diffuse skin thickening, and posterior shadowing are considered as the most consistent feature of malignancy.¹⁹ In our study, hypoechoic echo pattern was found to be a significant feature in distinguishing malignant from benign cases. However, MMG calcification was found to be the feature with the most potential in differentiating malignant lesions from benign. Our study also reported that calcification in malignant tumors was 5.05 times more compared to benign tumors. Grimm et al. have also reported that calcifications observed in ductal carcinoma in situ were significantly larger than in benign tumor (median, 10 mm versus 6 mm, respectively; p<0.001).²⁰

It was found that there were a few cases in our study, where MMG failed to pick up the features that were picked by ultrasound. There were three cases of infiltrating ductal carcinoma which were not defined much on MMG but ultrasound helped to delineate the lesions. There were three cases of intraductal papilloma, which was visualized as dilated ducts on ultrasound, but the lesion was not visualized on MMG. There was a case of fibroadenoma in a 24-year-old female which was reported as normal on MMG but was picked up on an ultrasound. Hence, our findings clearly demonstrate that SMG when conducted as an adjunct technique efficiently detects BC lesions which remain undetected through MMG.

In our study, the diagnostic accuracy of MMG along with SMG in detecting BCs was very good, specifically, for the BIRADS-4 (54 malignant cases) and BIRADS-5 lesions (9 malignant cases). Regarding BIRADS-3 lesions, the accuracy could be improved as some lesions proved to be malignant. The accuracy of BIRADS depends on the experience of radiologists. The present study added that the overall sensitivity of MMG combined with SMG in detecting BC was about quite similar; however, specificity was high compared to other studies. Khan et al in their study found that the overall sensitivity of MMG combined with USG was 94.67% and specificity was 77.78% in detecting BC.¹²

Limitations

The study has a few potential limitations. Firstly, in our study we were unable to characterize the microcalcifications based on their appearance and distribution such as cluster, popcorn, etc due to small sample size. Hence, studies in the future with a larger size is recommended to evaluate each characteristic subtype.

CONCLUSION

SMG used as an adjunct to MMG is proven as a reliable modality in detecting lesions that were not picked up on MMG especially for those of intraductal papilloma and duct ectasia.

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