



A Study on Characterization of Breast Lesions using Ultrasonography and Mammography and Assessing Its Accuracy by Comparing them with Histopathology

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Abstract

Introduction: Breast cancer is the most common cancer among women in India. It is very important to recognise the palpable breast lump as benign or malignant. The commonly used imaging modality in breast lumps are ultrasonography and mammography. The present study aims to find out the accuracy of sonomammography and mammography by comparing the results with histopathology.

Materials and Methods: A descriptive study was conducted among 75 female patients above 20 years of age with palpable breast lesions and bloody discharge from the nipple. Patients with advanced carcinoma, patients with history of previous breast biopsy and previously treated cases were excluded from the study. Designed as diagnostic test evaluation, sensitivity, specificity, positive predictive value and negative predictive value of the variables in differentiation was calculated comparing with histopathological diagnosis. The features of the tests was analyzed by Cohen's Kappa for statistical agreement with histopathology.

Results: In this study, the overall sensitivity and specificity of mammography obtained were 92%, and 87% respectively and that of sonomammography obtained were 83%, and 90% respectively for differentiating benign from malignant breast lesions.

Conclusion: This study shows that mammography and ultrasonography are useful in characterization of breast masses. Before going for biopsy, screening with mammography and sonomammography can be highly helpful.

Keywords: Benign, histopathology, malignant, mammography, sonomammography.

Introduction

A palpable breast lump is one of the common diagnostic problems. The most common cancer

among women in India is breast cancer.⁽¹⁾ The most important question in the case of a breast lump is whether the lesion is benign or malignant.

The field of breast imaging is undergoing a rapid revolution due to improvement in the technology. Ultrasonography is a commonly used screening imaging modality in breast lumps. It can be used in pregnant females also without the risk of radiation. It is important to obtain a definitive pre-operative diagnosis because the surgical approach is different in malignant and benign lesions. Breast cancer screening helps to detect cancers at an earlier, more treatable stage, and is an important clinical procedure because approximately one in eight women will develop breast cancer over their lifetimes. Improved technology and development of dedicated mammography units has given a new dimension to breast imaging, by decreasing the radiation dose and increasing the resolution. At the same time, development of high frequency probes allow a high degree of accuracy in characterizing breast lumps by ultrasonography.

Mammography is a radiographic examination that is designed for detecting breast pathology, particularly breast cancer. Breast cancer screening with mammography assists in detecting cancers at an earlier, more treatable stage, and is an important clinical procedure because approximately one in eight women will develop breast cancer over their lifetimes. High-quality mammography is the best diagnostic tool for the identification of breast calcifications. Technologic advances over the last several decades have greatly improved the diagnostic sensitivity of mammography.

Early X-ray mammography was performed with direct exposure film (intensifying screens were not used), required high radiation doses, and produced images of low contrast and poor diagnostic quality. Continuing refinements in screen-film technology and digital mammography, which entered the clinical arena in the early 2000s, further improved mammography⁽²⁾.

Mammography is the preferred method considered by many radiologists, for the reasons that high-quality mammography is the best diagnostic tool for the identification of breast calcifications.

Mammography technologists must be well trained and skilled in the proper positioning and compression of the breast.^(3,4)

Mammograms should be always interpreted on dedicated high-luminance mammographic view boxes or viewers, and a magnifying glass should be used routinely. Extraneous glare and light should be eliminated for optimal viewing conditions. Mammograms should be arranged in the same manner at each interpretation session to minimize left-right confusion. Routine mammograms should include craniocaudal (CC) and mediolateral oblique (MLO) views. That is, the two mammographic views usually obtained first for screening or diagnostic evaluations are the MLO view and the CC view. Magnification images of calcifications should be obtained in the CC and mediolateral (ML) or lateromedial (LM) views, also known as true lateral views. Tangential views are useful for verification of the intradermal location of calcifications⁽⁵⁾.

Other uses of mammography in evaluation of systemic diseases- although mammography is primarily used for the detection of breast cancer, it may reveal breast abnormalities related to extra-mammary disease such as congestive heart failure and central venous obstruction which may manifest as venous engorgement and breast edema. Pathologic arterial calcifications can be a factor for accelerated atherosclerosis such as chronic renal failure. Connective tissue diseases including rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis-polymyositis, and systemic scleroderma typically manifest with bilateral axillary lymphadenopathy, and stromal calcifications are also seen in the latter three disease processes. Some diseases such as neurofibromatosis type 1 and filariasis may manifest with pathognomonic findings at mammography, whereas other systemic diseases such as Wegener granulomatosis, sarcoidosis, and amyloidosis can manifest as non-specific breast masses that are indistinguishable from breast cancer and usually require tissue biopsy for confirmation⁽⁶⁾.

The characteristics suggestive of malignant lesions are: greater anteroposterior diameter, markedly hypo echoic nodule, presence of many microlobulations on the surface of a solid breast nodule, distal shadowing and the presence of punctate calcifications. Lucent-centered calcifications may be spiculated, with local thickening, branching, rod-like or angular. In early stages of development, calcifications in the wall of an oil cyst may simulate malignancy.⁽⁷⁾ Metastasis to the breast- Lymphoma and other hematologic malignancies, melanoma and lung cancer are the three most common blood-borne hematologic sources followed by ovarian cancer, soft tissue sarcomas and other gastrointestinal and genitourinary cancer⁽⁸⁾.

Breast abscess- Sonographic features suggestive of a breast abscess include- hypoechoic collection, mostly multiloculated, no vascularity within the collection, acoustic enhancement due to fluid content, an echogenic, vascular rim. Mammographic appearance can mimic carcinoma. A very few studies have been conducted regarding sonomammographic and mammographic findings of benign and malignant breast lesions and assessing how accurately it can be used by comparing them with the findings of the gold standard technique, histopathology. This study is an attempt to evaluate the accuracy of ultrasonography and mammography in characterizing breast lumps and comparing them with clinical findings and correlate them with histopathology results. It is very important to understand the accuracy of both diagnostic modalities as unnecessary and several biopsy can be avoided which itself can be a risk factor for breast cancer.

Aim

The aim of the study was to evaluate the mammographic and sonomammographic findings of the clinically palpable breast masses, to characterize the breast masses into benign and malignant and to compare categorized imaging findings with histopathology, as the gold standard.

Objectives

To determine the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of mammography and sonomammography in differentiating benign versus malignant breast lesion with histopathological correlation.

Material and Methods

A descriptive study was conducted among female patients with breast lesions at the Department of Radiodiagnosis, Government Medical College, Thiruvananthapuram for one year from July 2013 to July 2014. The study sample consisted of patients referred to Department of Radiodiagnosis for ultrasonogram and mammogram for evaluation of breast lesions.

All female patients above 20 years of age with palpable breast lesions and bloody discharge from the nipple were included for the study. Patients with advanced carcinoma (stage III and IV), previously treated cases and those with history of previous breast biopsy were excluded.

Consecutive sampling method was used for data collection using a pre-tested structured questionnaire. There were 75 patients satisfying the inclusion criteria during the study period. After obtaining the proper history, clinical examination and consent, the patients were subjected to ultrasound and mammography and was then compared with histopathology, which is the gold standard test. The need and aim of study were explained to the patients and informed written consent was obtained before including the subject in the study.

Data Collection

Patients who satisfied the inclusion criteria were subjected to undergo SS with 17mHz linear array probes and confirmed the findings with FNAC or biopsy reports. Data collection was started after obtaining the Institutional Research and Ethical Committee Clearance.

Benign criteria studied with mammography: 1. low density 2. smooth margins 3. coarse calcifications

Malignant criteria were: 1. High density 2. Spiculated margins 3. Micro calcifications 4. Perifocal haziness

Benign criteria studied with ultrasonography 1. Hyperechoic 2. Ellipsoid 3. Three or few lobulations 4. Thin echogenic capsules, and of malignant criteria were: 1. Anteroposterior diameter more than transverse 2. Angular margins 3. Markedly hypo echoic 4. Distal acoustic shadowing.

Data Analysis

Data was analysed using SPSS 16.0 and Microsoft Excel has been used to generate graph and tables. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of sonomammogram and mammography for

detection of benign and malignant breast lesions were worked out considering FNAC as the gold standard. It is derived from 2x2 tables with rows representing ultrasonography or mammography positive and negative cases as well as columns representing FNAC positive and negative cases. The features of the tests were analyzed by Cohen’s Kappa for statistical agreement between these and histopathology.

Results

The youngest patient was 23years and the oldest one was 67years old. 33.3% of them were in 50-59years age group, followed by 26.7% in 40 -49 years range and 18.7% in 30- 39 years range. 12% of the patients were of 60-69 years age group and 9.3% in 20-29 years age group.

Table 1: Distribution of benign and malignant cases according to margin

Margins	Malignant Number n (%)	Benign Number n (%)	Total (%)
Smooth	1(2.8)	28(71.8)	29(38.7)
Irregular	8(22.2)	10(25.6)	18(24)
Spiculated	27(75)	1(2.6)	28(37.3)
Total	39(100)	36(100)	75(100)

Table 2: Distribution of benign and malignant lesions according to shape with HPR correlation

Shape	Malignant Number n (%)	Benign Number n (%)	Total(%)
Ellipsoid	0(0)	26(66.7)	26(34.7)
Lobulated	1(2.8)	12(30.8)	13(17.3)
Angular	35(97.2)	1(2.6)	36(48)
Total	39(100)	36(100)	75(100)

P< 0.001

Table 3 Distribution according to benign criteria and negative predictive value of each characteristic in mammography

Character	FNAC		Total n (%)	Specificity	NPV
	Malignant n (%)	Benign n (%)			
Low density	2(5.6)	16(41.0)	18(24)	41.0	66.7
Smooth margins	1(2.8)	28(71.8)	29(38.7)	71.8	72.4
Macrocalcifications	1(2.8)	26(66.7)	27(36)	66.7	72.2

Table 4 Distribution according to malignant criteria and positive predictive value of each characteristic in mammography

Character	FNAC		Total n (%)	Sensitivity	PPV
	Malignant n (%)	Benign n (%)			
High density	34(94.4)	23(59)	57(76)	94.4	59.6
Spiculated	27(75)	1(2.6)	28(37.3)	75.0	96.4
Macrocalcifications	23(63.9)	0(0)	23(30.7)	63.9	100.0
Perifocal haziness	32(88.9)	13(33.3)	45(60)	88.9	71.1

Table 5 Distribution according to benign criteria and negative predictive value of each characteristic in ultrasonography

Criteria	FNAC		Total n (%)	Specificity	NPV
	Malignant n (%)	Benign n (%)			
Hyperechoic	2(5.6)	10(25.6)	12(16)	25.6	62.5
Ellipsoid	0(0)	26(66.7)	26(34.7)	66.7	74.9
Lobulated(3 or fewer lobulations)	1(2.8)	12(30.8)	13(17.3)	30.8	69.4
Thin echogenic capsule	9(25)	35(89.7)	44(58.7)	89.7	59.6

Table 6 Distribution according to malignant criteria and positive predictive value of each characteristic in ultrasonography

Criteria	FNAC		Total n (%)	Sensitivity	PPV
	Malignant n (%)	Benign n (%)			
Angular margins (spiculated)	35(97.2)	1(2.6)	36(48)	97.2	97.2
Distal shadowing	29(80.6)	3(7.7)	32(42.7)	80.6	90.6
Hypoechoic	34(94.4)	29(74.4)	63(84)	94.4	54.0
AP> Transverse	29(80.6)	3(7.7)	32(42.7)	80.6	90.6

Graph1 Distribution according to mammography, ultrasonography and histopathology

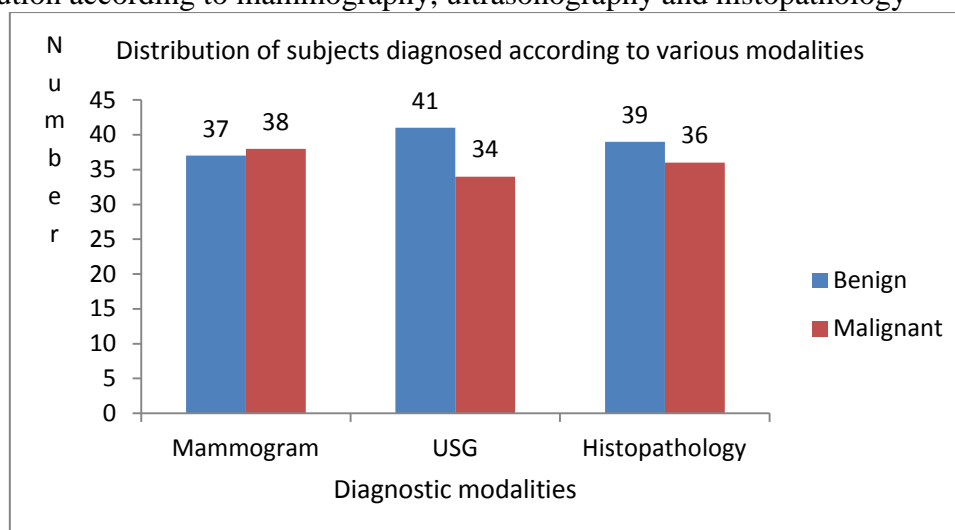


Table 7 Sensitivity, Specificity, PPV and NPV of mammography

Mammographic diagnosis	FNAC findings		Total n(%)
	Malignant n(%)	Benign n(%)	
Malignant(based on the presence of atleast 2 of the malignant criteria in mammography)	33(91.7)	5(12.8)	38(50.7)
Benign	3(8.3)	34(87.2)	37(49.3)
Total	36(100)	39(100)	75(100)

Measurement of agreement Kappa = 0.787, P< 0.001

With mammography, the sensitivity, specificity and accuracy obtained were 91.6%, 87.1% and 89.33% respectively for detection of malignancy

Table 8 Sensitivity, specificity, PPV and NPV of ultrasonography

Ultrasonographic findings	FNAC findings		Total n(%)
	Malignant n(%)	Benign n(%)	
Malignant(based on the presence of atleast 2 of the malignant criteria in ultrasonography)	30(83.3)	4(10.3)	34(45.3)
Benign	6(16.7)	35(89.7)	41(54.7)
Total	36(100)	39(100)	75(100)

Measure of agreement Kappa = 0.732 P< 0.001

With sonomammography, the sensitivity, specificity and accuracy obtained were 83.3%, 89.7% and 86.67% respectively for detetion of malignancy

Discussion

Breast lump is an alarming sign to women of any age and a diagnostic challenge to clinician and radiologist. The primary objective of our study was to assess the sensitivity, specificity, positive and negative predictive values of mammography and ultrasonography in differentiating benign and malignant breast lesions and comparing with histopathology. An observational study during a study period of one year from July 2013 to July 2014 was done. The study population consisted of 75 patients referred to Department of Radiodiagnosis for the evaluation of breast lesions. All patients with palpable breast lesions above 20 years of age were included in the study. Women in the age group of 20 – 70 years satisfying the inclusion criteria were included in the study group. Patients with advanced carcinoma, previously treated cases and those with prior histopathologic reports were excluded from the study. The maximum number of breast lumps was in the age group of 40- 49 years irrespective of benign or malignant nature. The most common benign lesion observed in the index study was fibroadenoma which was present in 16 patients (21 % of study population). According to literature, fibroadenoma is common before 40 years. In our study 10 out of 16 patients were below 40 years (62.5%).

The youngest patient with malignancy was 23 years old and the oldest patient was 67 years old. Above the age of 60 years, 4 out of 9 patients were malignant (44.5%) and rest were benign cases which consisted of oil cysts, simple cysts and breast abscesses. In our study, only 44.5% in the age group above 60 years were malignant. There is higher chance of malignancy in a breast lump in patients older than 60 years. This may be due to the advanced stage of presentation which was an exclusion criterion in our study.

According to histopathology, 39 lesions were benign and 36 lesions were malignant. Benign lesions that came across the study were simple cysts, breast abscess, galactocele and fibrocystic breast disease. Among the 6 cases of simple cyst,

3 were in the age group of 40- 49 years and 3 in 30-39 years. According to literature, cysts are common in 30- 50 years.

According to histopathology, 48% of all the lesions were malignant and 52% were benign. USS showed malignant features in 83.3% while mammography in 91.7%. 61.1% of carcinoma was located in upper outer quadrant and 16.7% in upper inner quadrant.

In this study 3 cases which were considered as benign lesions in mammography turned out to be malignant in histopathology. These lesions were mammographically categorized as benign because they were low density lesions with smooth margins (satisfying two benign criteria in mammography). 6 lesions which were considered benign in USS turned out to be malignant histopathologically. In USS these lesions were lobulated with smooth margins (satisfying two benign criteria in ultrasonography) and on histopathology they proved to be invasive ductal carcinoma. According to mammography results 49% were benign and 51% were malignant. 3 lesions which showed benign characteristics in mammography turned out to be malignant in histopathology. Those lesions were having lobulated margins and thin echogenic capsule. Histopathology of two of these lesions came out to be invasive ductal carcinoma and one invasive ductal carcinoma.

According to mammography 5 cases (12.8%) were diagnosed as malignant and proved to be benign in histopathology. 3 cases were having irregular margins and high density (satisfying 2 malignant criteria in mammography). USS of these lesions was favoring benign nature and histopathology showed fibroadenoma.

Two cases were showing perifocal haziness with high density (satisfying 2 malignant criteria in mammography) and proved to be abscess in histopathology.

According to the malignant criteria for ultrasonography, 4 cases which were diagnosed as malignant by USS came out to be benign on histopathology.

AP diameter was equal to transverse diameter in one of the case. Two lesions were hypoechoic and had angular margins (satisfying malignant criteria in ultrasonography) of which two turned out to be post-operative scar and other two turned to be benign epithelial hyperplasia. Post-surgical scar can mimic carcinoma but can be differentiated by the salient features like proximity of scar tissue to the incisional site, regression with time, planar configuration corresponding to the incisional plane rather than the three dimensional state.

According to benign criteria for ultrasonography 90% were benign. 6 cases which were diagnosed benign on ultrasonography came out to be malignant on histopathology. 2 were lobular carcinoma histologically. One was comedocarcinoma and 3 were invasive ductal carcinoma. Early malignancy may appear benign and can show well differentiated and smooth margins on ultrasonography.

Among the benign criteria for mammography 41% had low density. The low values in this study may be secondary to dense breast tissue in the respective cases. It is difficult to assess the character of lesion in mammography in patients with dense breasts (BIRADS 3 or 4 breast parenchyma). Other benign criteria for mammography in our study were smooth margins and presence of macro calcification. Among the benign criteria for mammography 72% of cases were having smooth margins on mammography with a NPV of 72. 28% of patients with smooth margins on mammography were histologically proven as malignant.

Those cases had other malignant features in mammography like calcifications and high density. Among the benign criteria for mammography 67% had macro calcifications and most of them were calcified fibroadenomas. The malignant criteria in mammography were high density, speculated margins, microcalcifications and perifocal haziness (if 2 or more criteria are satisfied it is taken as mammographically malignant). 64% of the cases showed micro calcifications. Positive predictive value of micro

calcification is 100% as all the cases with this finding were malignant. 95% of malignant cases showed high density. 75% had spiculated margins and 89% had perifocal haziness. The positive predictive value of high density, spiculated margins and perifocal haziness were 60, 96, and 71 respectively. Spiculated margins have high positive predictive value for malignancy in mammography. Benign criteria for USS were hyperechogenicity, ellipsoid shape, fewer lobulations and thin echogenic capsule (presence of 2 or more criteria). The negative predictive values of each were 62, 75, 70 and 60 respectively. Malignant criteria for ultrasound were angular margins, distal shadowing, marked hypo echogenicity and larger anteroposterior diameter (presence of 2 or more criteria). Positive predictive value were 97 for angular margins, 90 for distal shadowing, 54 for hypo echogenicity and 91 for larger anteroposterior diameter. With mammography, the sensitivity, specificity and accuracy obtained were 91.6%, 87.1% and 89.33% respectively for detection of malignancy. With sonomammography, the sensitivity, specificity and accuracy obtained were 83.3%, 89.7% and 86.67% respectively for detection of malignancy. Published data by Yang et al in 1996 in their study of 408 women with palpable breast lumps showed the following data:

Mammography: Sensitivity: 92%, Specificity: 94% and Positive predictive value: 84%

Ultrasonography: Sensitivity: 97%, Specificity: 97% and Positive predictive value: 85%

In this study the values obtained are-
Mammography: Sensitivity: 92%, Specificity: 87% and Positive predictive value: 87% and
Ultrasonography: Sensitivity: 83%, Specificity: 90% and Positive predictive value: 88%. These are comparable to the study quoted.

Benign criteria for USS were hyperechogenicity, ellipsoid shape, fewer lobulations and thin echogenic capsule (presence of 2 or more criteria). The NPV of each were 62, 75, 70 and 60 respectively. Malignant criteria for ultrasound were angular margins, distal shadowing, marked

hypo echogenicity and larger anteroposterior diameter (presence of 2 or more criteria). Positive predictive value were 97 for angular margins, 90 for distal shadowing, 54 for hypo echogenicity and 91 for larger AP diameter. With sonomammography, the sensitivity, specificity, PPV and accuracy obtained were 83.3%, 89.7%, 88% and 86.67% respectively for detection of malignancy which is similar to that of another study showed sensitivity: 97%, specificity: 97% and positive predictive value: 85%⁽⁹⁾.

Conclusion

In this study, the overall sensitivity, specificity, positive and negative predictive values of mammography and ultrasonography were calculated and it was found that mammography was more sensitive and specific in detecting malignant breast lesions. Those lesions with characteristic features of malignancy in mammography, like spiculated borders and microcalcifications with the branching pattern, can be considered as malignant and can be directly taken for surgery even without FNAC as these are more specific findings in malignancy and has a high positive predictive value. Together these imaging modalities can be reassuring if follow up is planned when the physical examination is not much suspicious and unnecessary breast biopsy can be avoided. The kappa values for mammographic and ultrasonographic diagnosis were 0.787 and 0.732 with P value <0.001 which indicates good agreement with histopathology. The possible clinical implications of the current study are that the ultrasonography and mammography together can be a useful diagnostic armamentarium for the clinician.

Limitation of the Study

Even though we have done ultrasonography and mammography, doppler evaluation of breast masses was not done which would have helped in better characterization of breast lesions into type of lesion i.e., benign or malignant. Also it is a

hospital based study, the result may not be representative of the general population.

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