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Original Research Article

Multimodality Evaluation of Breast Lesions

G David Chakravarthi[1], Riaz Mohammed[2*]

[1]Assistant Professor, Department of Radiodiagnosis, Government Medical College, Kadapa, Andhra Pradesh, India

[2]Assistant Professor, Department of Radiodiagnosis, Siddhartha medical College, Gunadala, Vijayawada, Andhra Pradesh, India

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Corresponding author: Dr. Riaz Mohammed

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Abstract:

Aim: To comparison of real time elastography, greyscale sonomammography and CR mammography and their correlation with FNAC/biopsy to differentiate the benign and malignant lesions of the breast.

Method:

A prospective study conducted in 80 Patients with complaint of pain or lump in the breast or nipple discharge those attending OPD/admitted at the Govt General Hospital for the 2 year duration. A Proforma used to collect the clinical and other relevant from all patients. Evaluation was done by mammography, sonomammography, elastography, MRI and correlated with FNAC/biopsy.

Results: Benign diseases (56.25%) were more common than malignant (43.75%), of which fibroadenoma is the most common lesion. Benign lesions are more common in below 50yrs age group. Incidence of malignant lesions is more in above 50yrs age group. Most common location for the lesions is upper outer quadrant (35%). In mammography, 30 lesions are malignant of which only 2 are benign in FNAC, whereas 50 lesions are benign of which only 7 are malignant. Mammography has a sensitivity of 80%, specificity of 95.5%, positive predictive value of 93.3%, and negative predictive value of 86%. Sonomammography has a sensitivity of 74.2%, specificity of 91%, positive predictive value of 86%, and negative predictive value of 82%. Real time Elastography has a sensitivity of 91.4%, specificity of 94.4%, positive predictive value of 94.1%, and negative predictive value of 91.8%. Combined CR mammography and sonomammography has a sensitivity of 82.8%, specificity of 93.3%, positive predictive value of 90.6%, and negative predictive value of 87.5%. Combined sonomammography and Real time Elastography has a sensitivity of 91.4%, specificity of 97.2%, positive predictive value of 96.96%, and negative predictive value of 92.1%. By combining all three modalities CR mammography, Greyscale Sonomammography and real time Elastography only two malignant lesions were misdiagnosed as benign and all benign lesions were correctly identified as benign. Combined Greyscale Sonomammography and real time Elastography do not have the disadvantage of radiation and it is easily available and easy to perform without any compression. Even in dense breasts the lesion can be identified easily.

Conclusion: Combination of CR mammography, Sonomammography and Real time Elastography has high diagnostic sensitivity and specificity in the diagnosis of benign and malignant breast masses obviating the use of higher modalities like MRI, CAD and Digital Tomosynthesis which is very useful.

Keywords: Sonomammography, Elastography, Biopsy, Breast Lesions, FNAC.

Introduction

Breast cancer is the most common of all cancers and is the leadingcause of cancer deaths in women worldwide, accounting for >1.6% of deaths and case fatality rates are highest in low-resource countries [1].

A study revealed that 1 in 28 women develop breast cancer during her lifetime. This is higher in urban areas being 1 in 22 in a lifetime compared to rural areas where this risk is relatively much lower being 1 in 60 women developing breast cancer intheir lifetime. [1] In India the average age of the high risk group in India is 43-46 years unlike in the west where women aged 53-57 years are more prone to breast cancer. [1]

If carcinoma breast is identified early and treated complete cure rate is possible. So multimodality imaging (mammography, ultrasound, elastography, MRI) of breast lesions will help in identifying malignancy early. By this, number of unnecessary invasive procedures (FNAC/biopsy) for benign lesions can be reduced and malignant lesions can be treated in early stage.

Breast cancer is the most common type of cancer in

women worldwide. [2]

Important clinical advances in breast Ultrasonography have the improved differentiation of benign/malignant solid breast lesions and the use of US to guide interventional procedures such as needle aspirations, core-needle biopsies, and pre-biopsy needle localizations of breast masses or calcifications. [3,4]

During the last few years, ultrasound contrast agents have been developed that increased blood echogenicity and improve ultrasound image quality by detection of slow and low volume blood flow in small tumor vessels (<5 mm) within the focal lesions in the breast. Commonly used contrast agents are Sonovue (sulfur hexafluoride microbubbles coated with phospholipids) and Levovist (galactose microparticles coated with palmitic acid). [5]

Ultrasound has also therapeutic role for targeted activation of delivered drugs in the form of microbubbles. [6]

Sonoelastography (SE) displays the relative stiffness of lesions compared with the stiffness of surrounding tissue and has high contrast with background breast tissue during deformation. Various techniques of elastography include stress strain elastogaraphy; shear wave elastography, acoustic radiation force impulse (ARFI) technique. It provides non-invasive evaluation of stiffness of the lesion thus differentiating less stiff benign from more stiff malignant lesions. This improves the specificity in identifying malignant lesions. [2]

Advantages of MR Mammography of the breast are that it can be used in women with denser breasts, in multi-focal cancers and to know the extent and spread, to check for recurrence of cancer, in women who have undergone lumpectomy, can see breast implants and look for ruptures. MR Mammography can distinguish mature scar from recurrence, in patients at high risk for developing breast cancer such as those with BRCA mutations or for indeterminate findings ona mammogram. [7]

Other MR related imaging techniques like Perfusion and diffusion imaging techniques and proton magnetic resonance spectroscopy (MRS)are also useful in differentiating between benign and malignant masses.

Invasive breast cancers demonstrate restricted diffusion (lower apparent diffusion coefficient) relative to normal breast tissue or benign breast lesions. This restricted diffusion of water in invasive cancers, renders these lesions bright on diffusion weighted images [13].

Elevated tCholine has been showing more frequently in malignant than in benign enhancing breast lesions. [8]

Positron emission tomography (PET) is limited by a lower sensitivity in detecting some breast tumors because of their small size, metabolic activity, histological subtype, microscopic tumor growth pattern and proliferation. [9] PET may be useful in identifying involved axillary nodes and distant metastases better than other imaging modalities.

Breast Specific Gamma Imaging (BSGI) addresses the limited tumor visibility of large field of view sestamibi imaging. It provides optimal spatial resolution and sensitivityand is targeted at 95% detection rate of lesions 5 mm in diameter. Despite all of these advances, it is still the case that no single imaging modality is capable of identifying and characterizing all breast abnormali ties and a combined modality approach will continue to be necessary. In this overview we evaluate the role of various imaging techniques in thediagnosis of breast cancer.

Aims & objectives of the study:

a) Comparison of real time elastography, greyscale sonomammography and CR mammography.
b) The effectiveness of radiological imaging to differentiate benign and malignant lesions.
c) Advantages of elastography over other imaging modalities (ultra-sound/ mammography).
d) To decrease invasive procedures (FNAC/biopsy).
e) To evaluate effectiveness of sonomammography and elastography as screening procedures.

Patients and Methods

Source of data

A prospective study conducted in 80 Patients with complaint of pain or lump in the breast or nipple discharge, attending OPD/admitted to the Government General Hospital, during 2020 July - 2022 June.

Method of collection of data

A Proforma drafted for the study of all patients with pain or lump in the breast, nipple discharge. Evaluation was done by mammography, sonomammography, elastography, MRI and correlated with FNAC/biopsy.

Sampling method: Simple random sampling

Mammography was performed with GE alpha st machine. Both craniocaudal and mediolateral views are taken and the image was assessed and scored using the BIRADS criteria.

Sonomammography and ultrasound Real Time elastography examination was performed with ESAOTE MY LAB class 3, which have real time elastography (stress -strain technique) with 5-10 MHz lineartransducer. Greyscale ultrasound

of both breasts was done by radial and grid scanning technique. The results were analyzed and categorized according to BIRADS (Breast Imaging Reporting and Data System) score.

RTE was performed by compression technique and score was given according to Italian Multi-Center Team of Study colour grading.[10] Colour coding in one ESAOTE machine was blue, green and red indicating hard, intermediate and soft areas respectively (as in classification) and in other machine was red, green, blue indicating hard, intermediate and softareas respectively.

In this classification score 1 lesions exhibit a typical three layer feature (blue–green–red from the surface to the bottom) usually indicative of cystic lesions. Score-2 is a benign-like lesion almost entirely green with random blue points. A score 3 is a lesion predominantly green showing some blue spots, consistent with benignity. Score 4 is an almost entirely blue lesion with minimal green points at the periphery, suspect for malig- Nancy. Score 5 is the same as in the Ueno classification, with an entirely blue lesion surrounded by a blue halo, consistent with malignancy.

MRI

MRI of breast was performed with 1.5T machine to find out how the lesions appear and whether there is any use in doing it. These imaging findings are correlated with FNAC/biopsy.

FNACs were performed under ultrasound guidance in the most suspicious lesions and at least two sites were taken. Core biopsy/excision biopsy was done when FNAC was inconclusive. Imaging studies were done for patients before FNAC.

Results

Incidence of breast lesions were more in >40 years i.e., 78.75%. Distribution of breast lesions was higher in Upper outer and upper inner quadrants i.e., 52.5%.

According to BIRADS classification, mammographic diagnosis revealed 11 cases in BIRADS-1, 19 cases in BIRADS-2, 20 cases in BIRADS-3, 20 cases in BIRADS-4, and 10 cases in BIRADS-5.

According to BIRADS classification, there were totally 38% of lesions were of malignant.

Sonomammography(USG) BIRADS revealed that 9 cases in BIRADS-1, 19 cases in BIRADS-2, 22 cases in BIRADS-3, 24 cases in BIRADS-4, and 6 cases in BIRADS-5. According to sonomammography classification, 38% of lesions were of malignant.

FNAC showed 43.75% of lesions were of malignant.

According to combined mammography and sonomammography diagnosis revealed 6 cases in BIRADS-1, 19 cases in BIRADS-2, 23 cases in BIRADS-3, 21 cases in BIRADS-4, and 11 cases in BIRADS-5. Combined mammography and sonomammography showed that 48.75% of lesions were of malignant. Elastography according to Italian multicentre team study Score classification, diagnosis revealed 8 cases in class-1, 9 cases in class-2, 21 cases in class-3, 21 cases in class-4, and 25 cases in class-5.

Elastography shows that 46.47% of lesions were of malignant. According to combined Sonomammography and Elastography according to BIRADS classification, diagnosis revealed 7 cases in BIRADS-1, 10 cases in BIRADS-2, 21 cases in BIRADS-3, 25 cases in BIRADS-4, and 8 cases in BIRADS-5.

Table 1: Association of mammographic diagnosis with FNAC; sonomammography diagnosis with FNAC; elastography with FNAC; Combined sonomammography and Elastography Diagnosis; Combined mammography and sonomammography Diagnosis

		FNAC diagnosis		Total	Sensitivity	Specificity	PPV	NPV
		Malignant	Benign					
Mammography Diagnosis	Malignant	28	2	30	80%	95.5%	93.3%	86%
	Benign	7	43	50				
Sonomammography Diagnosis	Malignant	26	4	30	74.2%	91%	86%	82%
	Benign	9	41	50				
Elastography Diagnosis	Malignant	31	2	33	88.5%	94.4%	93.9%	89.4 %
	Benign	4	34	38				
Combined sonomammography and Elastography Diagnosis	Malignant	32	1	33	91.4%	97.2%	96.96 %	92.1 %
	Benign	03	35	38				
Combined mammography and sonomammography Diagnosis	Malignant	29	3	32	82.8%	93.3%	90.6%	87.5 %
	Benign	06	42	48				

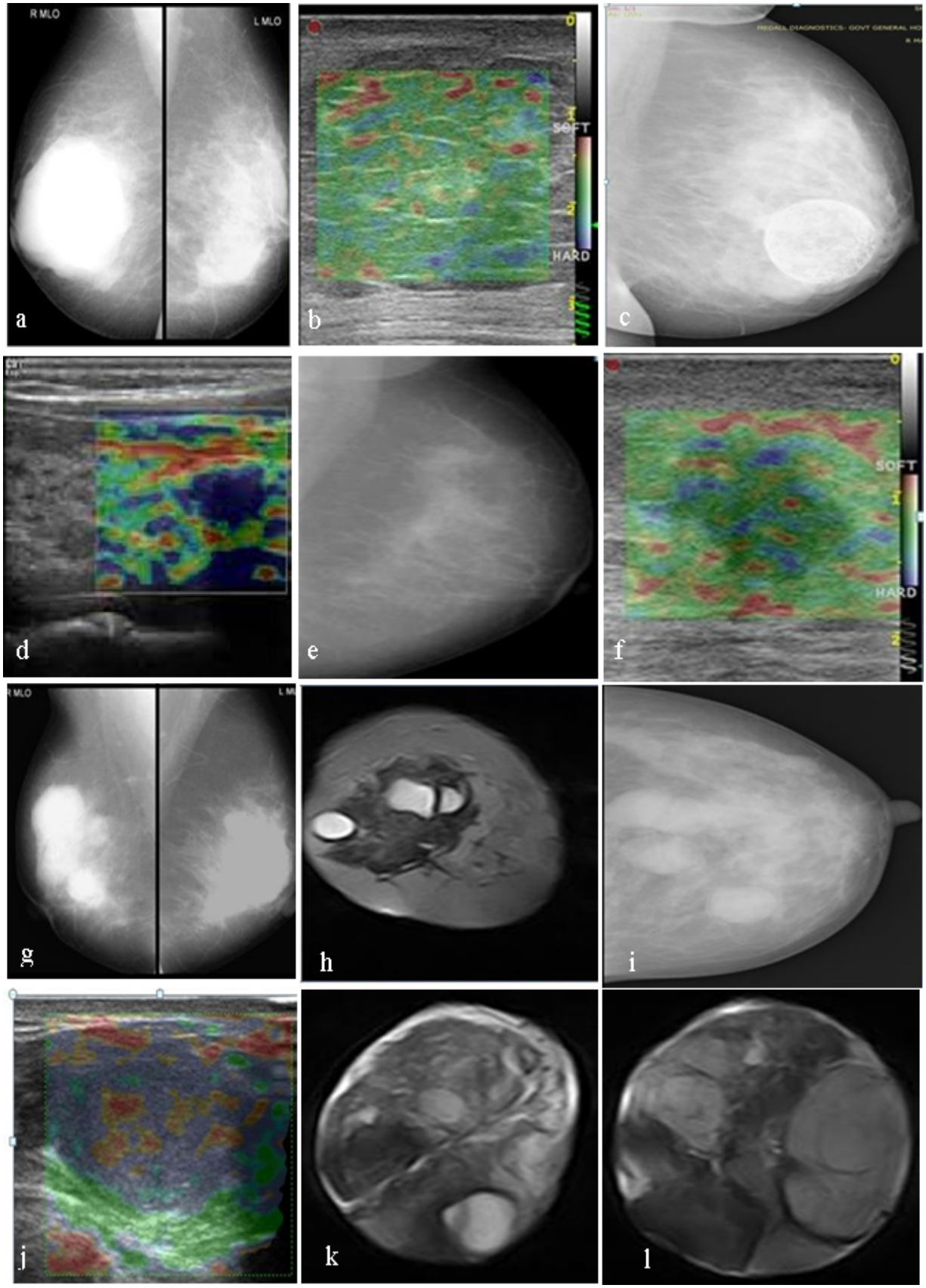

Figure 1: a. Giant fibroadenoma -RT and LT MLO, b. Giant fibroadenoma -B mode US, c. Oilcyst –MLO view, d. Oilcyst –UE. e. DCIS-LT MLO, f. DCIS-LT UE, g. Fibrocystic disease -RT MLO and LT MLO, h. Fibrocystic disease -T2W MRI. i. Multiple fibroadenomas- LT CC. j. Multiple fibroadenomas –UE, k. Multiple fibroadenomas-T2W MRI, l. Multiple fibroadenomas-T1W MRI.

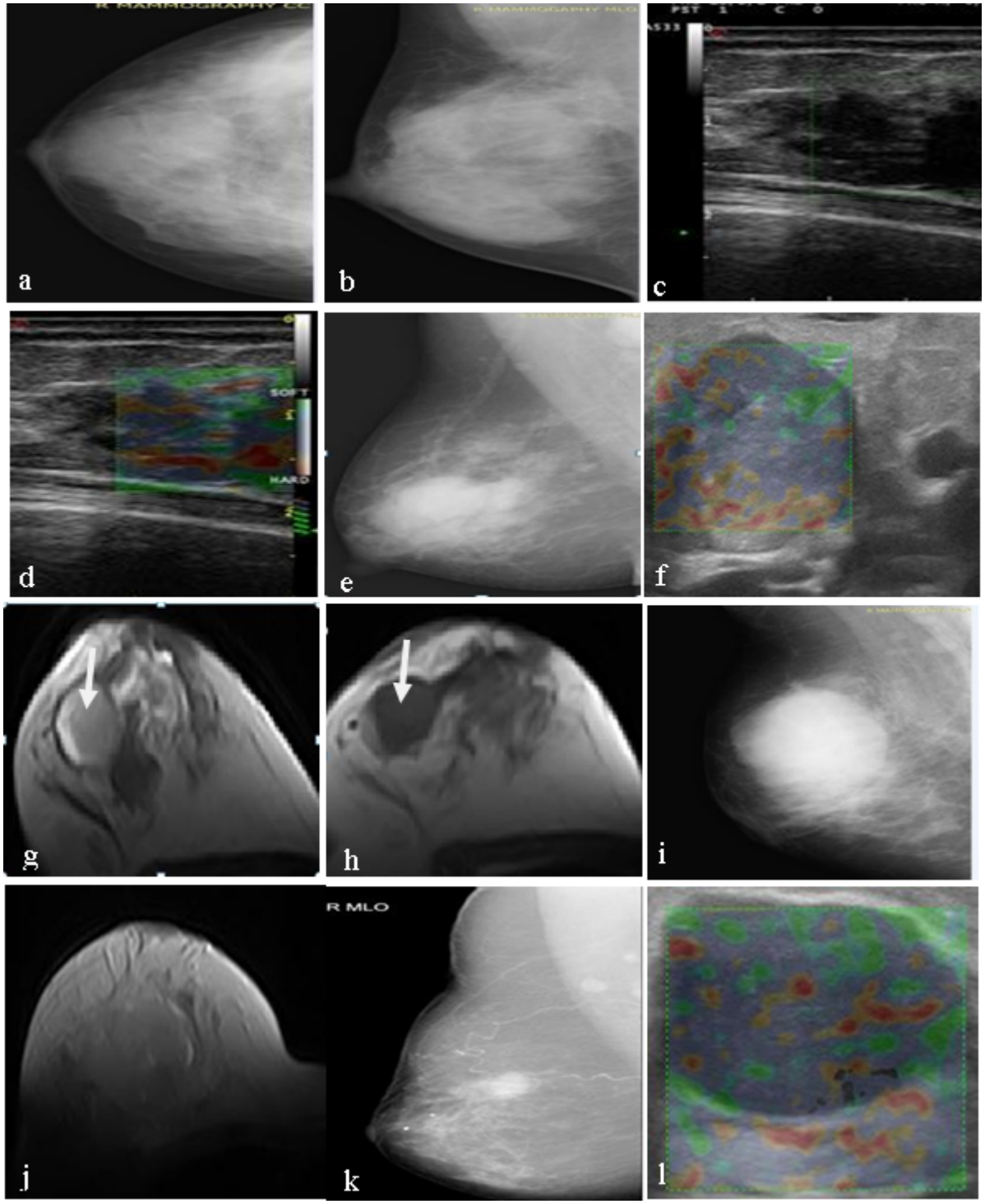

Figure 2: a. Sclerosing adenosis-RT CC, b. Sclerosing adenosis -RT MLO, c. Sclerosing adenosis-B Mode US, d. Sclerosing adenosis-RT MLO, e. Papillary carcinoma-RT MLO, f. Papillary carcinoma-UE, g. Papillary carcinoma-T2W MRI , h. Papillary carcinoma--T1W MRI . i. Intraductal carcinoma –RT MLO, j. Intraductal carcinoma-T2W MRI. k. Medullary carcinoma –RT MLO, l. medullary carcinoma - B mode US.

Discussion

In India the average age of the high risk group is 43-46 years unlike in the west where women aged 53-57 years are more prone to breast cancer. [1] Presently, 4% are in 20 to 30 yrs age group, 16% are in 30 to 40, 28% are in 40 to 50 age group. 48% patients are below 50. An increasing number of patients are in the 25 to 40 years of age, and this definitely is a very disturbing trend. [11]

In our study, the incidence of breast lesions was more in >40 years i.e., 78.75% and remaining 21.25% were of below <40 yrs age group. Below

50 yrs, out of 48 cases, 13 (37%) were malignant and 35 were benign and above 50yrs out of 32 cases 22 (63%) were malignant and 10 were benign indicating increased incidence of malignancy with increasing age.

In our study, the most common symptom of presentation was lump in the breast seen in 77 patients and the second most common symptom was pain seen in 37 patients. Lesions were most commonly located in the Upper outer quadrant 35% cases and 17.5% cases in Upper inner quadrant.

Marshall et al. suggested that 60% of their cases had the tumor in the upper outer quadrant while Sen and Dasgupta had 49% of the cases in same quadrant. [12,13]

Of the benign lesions fibroadenoma was the most common histopathological diagnosis in the present study. Of the malignant lesions intraductal carcinoma was the most common histopathological diagnosis inthe present study.

In a study by Nesreen Mohey et al [14] mammography has sensitivity 72.7% and specificity 86.4%. In the present study mammography has a sensitivity of 80%, specificity of 95.5%, positive predictive value of 93.3%, and negative predictive value of 86% which are higher than previous studies.

However, the false negative rate of mammography for breast cancer in patients with palpable abnormalities of the breasts has been reported to be as high as 16.5%. [15]

In the present study sensitivity, specificity, PPV, NPV were 74.2%, 91%, 86%, 82% respectively. When compared to Sabine et al [16] study which had sensitivity, specificity, PPV, NPV 89.1%, 79.1%, 65.7%, 90.9% respectively, present study has higher specificity and PPV. When compared to Marwa et al [17] study that had sensitivity, specificity, PPV, NPV 85%, 94%, 92.5%, 88% respectively, all the values are lower in the present study.

All solid masses may not be visible in the sonomammography even in dense breasts. A palpable mass that is invisible in both mammography and sonography strongly needs biopsy histology. When compared to mammography, sonomammography has lower sensitivity, specificity, PPV and NPV. In 11 cases no lesion was detected in mammogram and in 9 cases no lesion was detected in sonomammogram. In 5 cases lesion was found in sonomammogram that were not detected in mammogram. Of these 5 cases 2 were fibroadenomas, 2 were fibrocystic disease, and 1 duct ectasia. Sonomammography is very useful in dense breasts and can be used as screening for the breast lesions in younger women and women with dense breasts.

In 3 cases, lesions were found in mammogram that were not de- tected in sonomammogram, these three were fibroadenomas. This may be due to isoechoic appearance of fibroadenoma with adjacent breast tissue.

In 6 cases, no lesion was detected in both sonomammography and mammography; FNAC was done which showed 1 fibroadenoma, 3 fibroadenosis changes, and 2 normal breast tissues.

In the present study sensitivity, specificity, PPV and NPV of elastography are 88.5%, 94.4%, 93,9%,89.4%. When compared to sonomammography, elastography had higher sensitivity in Itoh et al [18] study, but higher specificity in many other studies. As in several studies, elastography showed higher specificity than sonomammography in the present study.

But many studies showed lower sensitivity. In the present study both sensitivity and specificity were higher than sonomammography which is consistent with Leong et al. study in which sensitivity and spe cificity were 88.5% and 42.9%, respectively for conventional ultrasound, 100% and 73.8%, respectively for elastography.

In present study, sensitivity, specificity, PPV and NPV for the com- bination of sonomammography and UE were higher than those of sono-mammography alone. Compared with mammography, UE has higher sensitivity and NPV but slightly lower specificity. But combined UE and sonomammography has higher sensitivity, specificity, PPV and NPV than mammography alone or combined mammography and sonomammography.

There is an overlap of the elasticity between benign and malignant lesions in the breast, which limits the use of UE. In the present study, 4 out of 35 cancers were missed (false-negative) by UE. False-negative findings on UE were DCIS, medullary carcinoma, papillary carcinoma and large intraductal carcinoma with necrosis. Two (large IDC with necrosis and DCIS) of the four were detected as malignant by mammography, and two (including 1 medullary carcinoma and 1 papillary carcinoma) were missed by all 3 modalities.

2 out of 36 benign lesions were misdiagnosed by UE. Among the false positive diagnoses, one was a oil cyst with calcification, that in- creased the stiffness, and one was a involuting fibroadenoma with calcifications, which increased the hardness of the lesion. Therefore, when using UE, one should pay attention to all the factors that would affect the stiffness of lesions and cause misleading results. In these cases, mammography was very useful as it can detect benign calcifications easily and downstaged to BIRADS II (i.e benign).

In mammography, 2 out of 45 benign lesions were misdiagnosed asmalignant (false positive), one was sclerosing adenosis which on sonomammography also misdiagnosed as malignant but elastography correctly identified it as benign soft lesion. Another one was Fibroadenoma which on sonomammography and elastography correctly identified as benign lesion.

In sonomammography 9 out of 35 (false negatives) malignant lesions were missed. Four were correctly identified in mammography, but by using elastography three more lesions were diagnosed as a malignant. So, by combining all the three modalities only two lesions were missed.

In sonomammography, 4 out of 45 benign lesions were misdiagnosed as malignant (false positive). These are 1 sclerosing adenosis, 2 fibroadenomas, 1 chronic abscess. Both mammography and sonomammography misdiagnosed sclerosing adenosis as malignant but elastography showed score 2 thus differentiating it as a benign lesion. Of 2 cases of Fibroadenomas, one was correctly identified as benign by elastography and mammography, and other was correctly identified by elastography but mammography misdiagnosed it as malignant. Chronic abscess was correctly identified as benign by elastography and mammography.

MRI was also performed wherever necessary to know how the lesion appears in MRI. Cystic lesions appeared as T2 and fat sat hyperintense, T1 hypointense lesions, fibroadenomas appear as well defined T2 iso to hyperintense (but less than fluid signal), T1 hypointense lesion. Malignant lesions have nonspecific findings.

On comparison of CR mammography, greyscale sonomammography and real time elastography, CR mammography has highest specificity, whereas real time elastography has highest sensitivity, PPV and NPV.

By combining all three modalities CR mammography, greyscale sonomammography and real time elastography, only two malignant lesions were misdiagnosed as benign and all benign lesions were correctly identified as benign. So, multimodality imaging approach can increase sensitivity, specificity, PPV and NPV. So, by identifying benign lesions correctly, unnecessary FNACs/biopsies can be avoided.

UE has advantages of using no radiation, simple to use, it can be overlapped on the greyscale ultrasound image, identifies cyst with more specificity (three layer pattern), able to differentiate BIRADS 3 and 4 lesions. In the present study UE is superior to conventional sonography and is superior or equal to mammography in differentiating benign and malignant lesions in the breast. By combining UE and sonography, the detection accuracy can be improved greatly, and the combination potentially could reduce unnecessary biopsy. This combination was the optimal modality in the present study.

Conclusion

Real-time Elastography, which is cheap, easier to operate and has no radiation, is an useful adjunct technique to ultrasound for the characterization of benign and malignant solid lesions as it increases the diagnostic sensitivity and specificity comparable to Sonomammography or mammography alone.

So combination of Sonomammography and Real time Elastography can be used as a screening procedure to differentiate benign and malignant lesions in young women and women with dense breasts wheremammography cannot be used or less sensitive.

Sonomammography is better to identify cystic lesions. Further specificity can be increased by using Real time Elastography.

Further Real time Elastography is useful to obtain representative samples from the suspicious areas within the lesion thus reducing unnecessary tissue injury and increases the specificity of diagnostic sampling. As real time Elastography is qualitative technique and operator de- pendant, accuracy can be increased by using quantification techniques like shear wave elastography, acoustic radiation force impulse (ARFI) techniques.

Combination of CR mammography, Sonomammography and Realtime Elastography has high diagnostic sensitivity and specificity in the diagnosis of benign and malignant breast masses obviating the use of higher modalities like MRI, CAD and Digital Tomosynthesis which is very useful. But major limitation is combination of CR mammography; Sonomammography and real time Elastography cannot quantify the disease burden (no. of lesions) correctly and is inferior to dynamic MRI.

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