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Comparative Study between Accuracy of Mammography and USG in Preoperative Assessment of Breast Cancer

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Abstract: ***Breast cancer is the second most common cause of death from cancer in women. The aim of this study was to determine which is more accurate imaging test mammography or ultrasound for diagnosis of breast cancer based on the women's age and breast density. We examined 40 patients with breast symptoms, by clinical breast examination, mammography and ultrasound. A total of 40 breast lesions were examined by histopathology analyses. Sensitivity varied significantly with age and breast density. In the 20 women who had both tests, ultrasound had a higher sensitivity than mammography in women younger than 50 years, whereas mammography had a higher sensitivity than ultrasound in women older than 50 years. The sensitivity according to age was 12.5% for mammography and 17.5 % for ultrasound. Comparing the sensitivity of mammography and ultrasound according to the breast density indicates that mammographic sensitivity was 20% among women with predominantly fatty breast, but 5% in women with heterogeneous dense breasts, with the increase of fibro glandular density the level of sensitivity with mammography decreases, while ultrasonography sensitivity was 5% among women with predominantly fatty breast and 30% for heterogeneous dense breasts.***

Keywords: breast cancer, diagnostic methods, mammography, ultrasound, age

1. Introduction

Breast cancer is the most common type of cancer in women today, accounting for 1 of every 3 cancers diagnosed. A woman's chance of developing invasive breast cancer at some time in her life is approximately 1 in 8 (12%). It is one of the leading causes of cancer mortality among women [1]. Breast cancer is a heterogeneous disease with multiple causes. Epidemiological studies have identified many risk factors that increase the chance for a woman to develop breast cancer. Important risk factors for female breast cancer include early age at onset of menarche, late age at onset of menopause, a first full-term pregnancy after the age of 30 years, a history of premenopausal breast cancer for a mother and a sister, and a personal history of breast cancer or benign proliferative breast disease. Obesity, nulliparity, and urban residence have also been associated with an increased risk of breast cancer. Mammography plays a major role in early detection of breast cancers, detecting about 75% of cancers at least a year before they can be felt. There are 2 types of mammography examinations: screening and diagnostic. Screening mammography is done in asymptomatic women. Early detection of small breast cancers by screening mammography greatly improves a woman's chances for successful treatment. Screening mammography is recommended every 1-2 years for women once they reach 40 years of age and every year once they reach 50 years of age. In some instances, physicians may recommend beginning screening mammography before age 40 if the woman has a strong family history of breast cancer. Studies have shown that regular mammograms may decrease the risk of late-stage breast cancer in women 40 years of age and older [(2,3).] Diagnostic mammography is performed in symptomatic women, when a breast lump or nipple discharge is found during self-examination or an abnormality is found during screening mammography. Diagnostic mammography is more involved and time-consuming than screening mammography and is used to determine exact size and location of breast abnormalities and to image the surrounding tissue and lymph nodes. Mammography is known to a have a certain false-negative rates. According to data from the Breast Cancer Detection Demonstration Project, the false-negative rate of mammography is approximately 8 to 10 %. Approximately 1 to 3 % of women with a clinically suspicious abnormality, a negative mammogram, and a negative sonogram may still have breast cancer. Possible causes for missed breast cancers include dense parenchyma obscuring a lesion, poor positioning or technique, perception error, incorrect interpretation of a suspect finding, subtle features of malignancy, and slow growth of a lesion.(4). Ultrasonography has been playing an increasingly important role in the evaluation of breast cancer. Breast ultrasound is the preferable method in the case of a symptomatic patient, after clinical examination. In the case of a patient without symptoms, breast ultrasound is ascribed a higher sensitivity for detecting breast cancer in women with dense breast tissue, women under the age of 50 and high-risk women. Many specific indications for breast US have been enumerated, including:evaluation of a palpable mass in-completely evaluated at mammography;differentiation of a cyst from a solid nodule; evaluation of palpable lesions with associated mammographic asymmetry, no mammographic findings, the presence of implants, or a history of lumpectomy or segmentectomy. Mammographically occult cancers can be detected by ultrasound in 10 to 40% of the cases depending on the patient's breast density and age [5,6,7].The aim of this study was to determine which is more accurate imaging test mammography or ultrasound for

diagnosis of breast cancer based on the women's age and breast density.

2. Material and Methods

In Department of Surgery in JSS Hospital, Mysuru, between October 2014 to July 2016we examined 45women with breast symptoms.The mean age of the patient was 54.2 years, standard deviation (SD) 11.2 (age range 37 to 75 years). Breast lesions were detected by clinical breast examination, mammography and ultrasound. A total of 40 breast lesions were identified as Ca breast histological methodology. Histopathology results revealed the presence of 40 invasive cancers, and 5 benign lesions, which were excluded from study.

Anamnesis:
To each patient, detailed history was taken including: Age at first childbearing, age at menarche, age at menopause, history of breastfeeding, number of children,history of hormone therapy, a history of premenopausal breast cancer for a mother and a sister, a personal history of breast cancer or benign proliferative breast disease, radiation, chemical exposure and smoking.

Analysis in detail:
The protocol ofdiagnosis consisted of clinical breast examination, ultrasound, mammography and histopathological examination.

Physical examination
Clinical breast examination of the whole breasts and axillary's regions was performed with the patient in the sitting position with arms both lowered and raised. In an upright position, we visually inspects the breasts, noting asymmetry, nipple discharge, obvious masses, and skin changes, such as dimpling, inflammation, rashes, and unilateral nipple retraction or inversion. With the patient supine and one arm raised, we thoroughly palpates breast tissue, axillary's region and supraclavicular area, assessing the size, texture, and location of any masses. After the patient history is obtained and the clinical breast examination is performed, the next diagnostic step was mammography, ultrasound and biopsy.

Mammography
Conventional film-screen mammography was performed with at least two views per breast, medio-lateral oblique and cranio-caudal views. Additional views or spot compression views were obtained where appropriate. Mammograms were obtained with dedicated mammography units (Alpha RT Imaging, General Electric Medical Systems, Milwaukee). Mammograms were interpreted according to the Breast Imaging Reporting and Data system (BI-RADS)diagnostic categories on a five-point scale, with BI-RADS 1 (negative), 2 (benign finding), 3(probably benign), 4 (suspicious abnormality), and 5 (suggestive of malignancy).

Breast Ultrasound
The radiologist who had performed the physical examination and who had interpreted the mammograms of that patient performed breast ultrasound. Ultrasound examinations were performed using a high-resolution unit (AlokaSSD ; Tokyo, JapanandMindray DP Plus) with a linear array probe centred at 7.5 MHz. All ultrasound examinations were performed with the patient in a supine position for the medial parts of the breast and in a contra lateral posterior oblique position with arms raised for the lateral parts of the breast. The whole breasts were scanned. Diagnoses were scored on a five-point scale identical to the mammographic BI-RADS categories (8).

Histopathological examination
A total of 40 breast lesions were turned out to be Ca breast by histological methodology. Final histologic diagnosis was obtained for all patients who underwent surgical biopsy, and all cases were verified by reviewing the histopathology report. Histopathology results revealed the presence of 37 invasive ductal cancers and 3 were lobular carcinoma. The 5 benign cases were excluded as per exclusion criteria.

Therapy
Treatment of patient with breast cancer was based on a multimodality approach combining surgery, radiation therapy hormonal therapy and/or chemotherapy. Treatment is tailored for an individual patient based on tumor size, axillary lymph node involvement, oestrogens and progesterone status, histologic tumour type, standardized pathologic grade, and menopausal status.

Statistical analysis
X^2 test, and student t-test were used for statistical data processing. The significance of differences observed was assessed using Pearson's chi-square test, with $p<0.05$ considering to be statistically significant.

3. Results

Cases selected according to inclusion and exclusion criteria.
History noted and clinical examination was done.
Consent was taken
Investigation – mammography, USG – Breast, FNAC/Biopsy
Comparison of diagnostic accuracy between Mammography and USG with FNAC / Biopsy of the same patientswas done
The histopathology has been used as a gold standard for confirming the diagnosis in operated cases

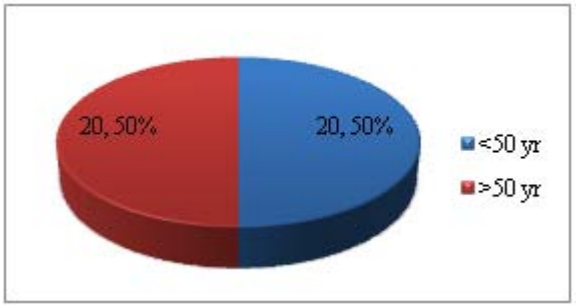
Age Distribution

40 case minimum age of 37yrs old and maximum age of 75 yrs were taken for studies with mean 54.3 and median 50.5 with standard deviation 11.2

	Mean	Median	Standard Deviation
Age yr	54.3	50.5	11.2

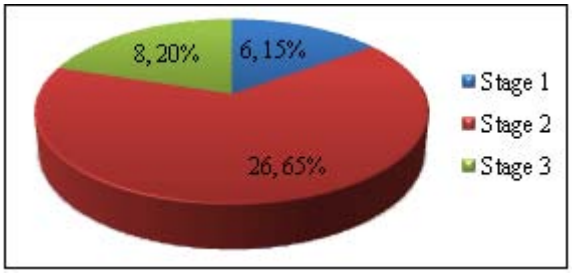
Out of 40 cases 20 were less than 50 years of age and 20 were more than 50 years of age

		Count	Column N %
Age category	<50 yr	20	50.0%
	>50 yr	20	50.0%



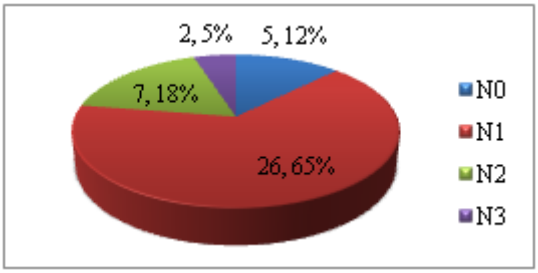
Clinically cases classified as per TNM staging.
65% of cases were T2

		n	%
T_stage	Stage 1	6	15.0
	Stage 2	26	65.0
	Stage 3	8	20.0



65% cases were N2

		Count	Column N %
N stage	N0	5	12.5%
	N1	26	65.0%
	N2	7	17.5%
	N3	2	5.0%



Maximum cases observed were T2 N1

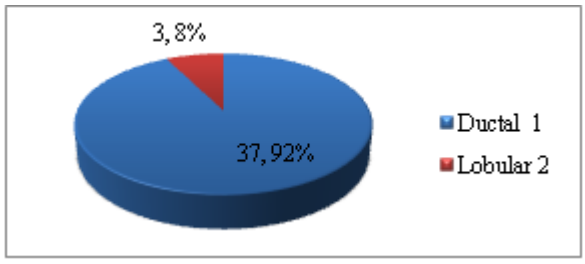
		N_stage							
		.00		1.00		2.00		3.00	
		Count	%	Count	%	Count	%	Count	%
T stage	1.00	1	20.0%	3	11.5%	2	28.6%	0	.0%
	2.00	3	60.0%	18	69.2%	4	57.1%	1	50.0%
	3.00	1	20.0%	5	19.2%	1	14.3%	1	50.0%

		N stage							
		N0		N1		N2		N3	
		n	Total %	n	Total %	n	Total %	n	Total %
T stage	T1	1	2.5	3	7.5	2	5.0	0	.0
	T2	3	7.5	18	45.0	4	10.0	1	2.5
	T3	1	2.5	5	12.5	1	2.5	1	2.5

Histopathological analysis

Maximum case (37 out of 40) were ductal carcinoma and three were lobular carcinoma

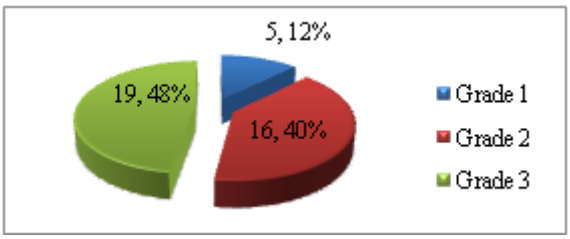
		Count	Column N %
type	Ductal 1	37	92.5%
	Lobular 2	3	7.5%



The grading of tumor done as per Bloom Richardson's classification.

		Count	Column N %
grade	Grade 1	5	12.5%
	Grade 2	16	40.0%
	Grade 3	19	47.5%

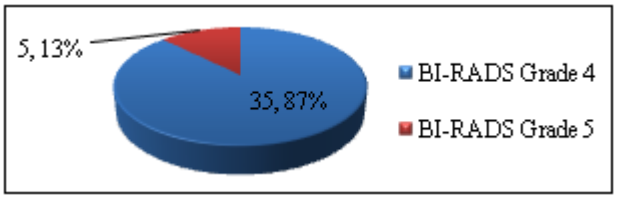
47.5 % cases were grade 3

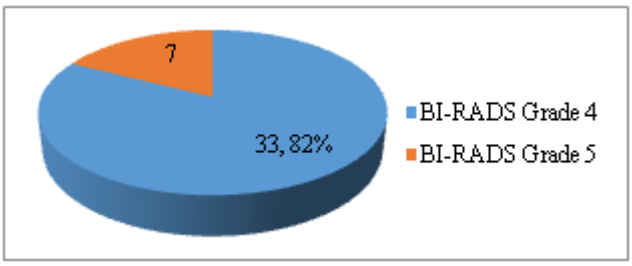


The Mammography reports collected. The BI- RADS classification used to grade.Only two grades were observed.Grade 4 suggested suspicious lesion while Grade 5 suggested confirmatory carcinoma. 12.5% cases showed confirmatory carcinomatous lesion

		n	%
Mamography	BI-RADS Grade 4	35	87.5
	BI-RADS Grade 5	5	12.5

		n	%
USG	BI-RADS Grade 4	33	82.5
	BI-RADS Grade 5	7	17.5





The USG reports of the same patients collected. The lesions are graded as per BI – RADS classification. 17.5 % cases confirmed the carcinomatous lesion.

Comparison of Mammography and USG

MAMOGRAPHY * USG Crosstabulation				
		USG		
		BI-RADS Grade 4	BI-RADS Grade 5	Total
MAMOGRAPHY	BI-RADS Grade 4	29	6	35
	BI-RADS Grade 5	4	1	5
Total		33	7	40

Kappa=0.024, p=0.9

Crosstabulation between USG and mammography, the p value is not significant. While kappa coefficient showed there is slight agreement between them. But if we divide the cases according to age as less than 50 & more than 50, the more value of kappa more than 50 yrs shows there is fair agreement between them.

MAMOGRAPHY * USG Crosstabulation						
			USG			Kappa and p
age_But if			BI-RADS Grade 4	BI-RADS Grade 5	Total	
<50	MAMOGRAPHY	BI-RADS Grade 4	13	6	19	K=-0.094 P=0.5
		BI-RADS Grade 5	1	0	1	
	Total		14	6	20	
>50	MAMOGRAPHY	BI-RADS Grade 4	16	0	16	K=-0.35 P=0.04
		BI-RADS Grade 5	3	1	4	
	Total		19	1	20	

When mammography is compared with HPE (gold standard) 12.5 % cases showed grade 5 lesion suggesting confirmatory diagnosis.
The sensitivity estimated the same.
Specificity could not be commented as benign lesions were excluded from study.

Comparison of mammography with histopathology

		Confirmed Ca
		Count
MAMOGRAPHY	Suspicious Ca	35
	Highly suspicious of Ca	5

Parameter	*Estimate*	*Lower - Upper 95% CIs*
Sensitivity	12.50%	5.459, 26.11
Positive Predictive Value	100%	56.55, 100
Negative Predictive Value	0.00%	0.0, 9.89
Diagnostic Accuracy	12.50%	5.459, 26.11

Comparison of mammography with histopathology in different ages

				histopathology	
				Suspicious Ca	Highly Suspicious Ca
				Count	Count
Age	<50 yr	MAMOGRAPHY	Suspicious Ca	0	19
			Highly suspicious of Ca	0	1
	>50 yr	MAMOGRAPHY	Suspicious Ca	0	16
			Highly suspicious of Ca	0	4

<50 yr

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	5	(0.8881, 23.61[1])
Positive Predictive Value	100	(20.65, 100[1])
Negative Predictive Value	0	(0.0, 16.82[1])
Diagnostic Accuracy	5	(0.8881, 23.61[1])

>50 yrs

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	20	(8.066, 41.6[1])
Positive Predictive Value	100	(51.01, 100[1])
Negative Predictive Value	0	(0.0, 19.36[1])
Diagnostic Accuracy	20	(8.066, 41.6[1])

The sensitivity of mammography more than 50 % of patients was 20 %
Comparison of USG with histopathology in different ages

When USG is compared with HPE (gold standard)
17.5 % cases showed grade 5 lesion suggesting confirmatory diagnosis.
The sensitivity estimated the same.
Specificity could not be commented as benign lesions were excluded from study.
While sensitivity in less than 50 % of cases was 30 %.

				Histopathology	
				Suspected Malignant	Malignant
age_c	<50 yr	USG	Suspected Malignant	0	14
			Malignant	0	6
	>50 yr	USG	Suspected Malignant	0	19
			Malignant	0	1

<50 yr

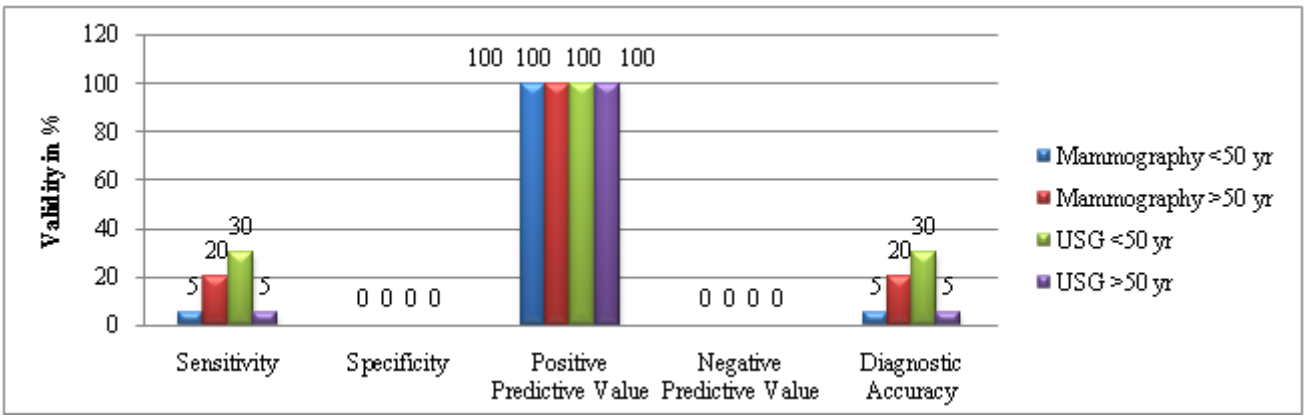
Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	30	(14.55, 51.9[1])
Positive Predictive Value	100	(60.97, 100[1])
Negative Predictive Value	0	(0.0, 21.53[1])
Diagnostic Accuracy	30	(14.55, 51.9[1])

>50 yr of age

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	5	(0.8881, 23.61[1])
Positive Predictive Value	100	(20.65, 100[1])
Negative Predictive Value	0	(0.0, 16.82[1])
Diagnostic Accuracy	5	(0.8881, 23.61[1])

Total USG with histopathology

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	17.5	(8.745, 31.95[1])
Positive Predictive Value	100	(64.57, 100[1])
Negative Predictive Value	0	(0.0, 10.43[1])
Diagnostic Accuracy	17.5	(8.745, 31.95[1])



4. Discussion

Breast cancer, is an important health problem in India. In the last decades there is little increasing of knowledge and development of breast cancer management, which resulted in increasing of mortality rates from breast cancer. All women are at risk for developing breast cancer. The older a women is, the greater her chances of developing breast cancer. Approximately 77% of breast cancer cases occur in women over 50 years of age. Most important factor in reducing death from breast cancer is early detection. Early detection and treatment is a key to preventing breast cancer from spreading. Mammography and ultrasound are the standard imaging techniques for detection and evaluation of breast disease . Women who present with breast symptoms or who have palpable findings on clinical examination are usually investigated with breast imaging, which generally consists of mammography or breast ultrasound or both. The choice of primary breast imaging in examining women with symptoms is partly based on age. However, despite the importance of age in clinical practice, little evidence exists as to the appropriate age that delineates the choice of initial diagnostic breast imaging in symptomatic women. In the absence of evidence, experts suggest that women younger than 45 years be examined with ultrasound, and women 45 years and older be examined with mammography, as the primary breast imaging modality.

In our study which was a prospective comparative study, patients presenting to JSS medical college and hospital who satisfied the inclusion and exclusion criteria were taken into the study after obtaining an informed written consent from

them. They were then examined clinically and when the findings seemed to be malignant they were made to undergo imaging modality (sonogram and mammogram). Same patients underwent surgery and HPE report was obtained.

In our data we show a progressive improvement in sensitivity of mammography in women 50 years or older relative to younger women, that has been shown in other studies(11,12,13,19,20).However, in women 50 years or younger, ultrasound has a significantly greater sensitivity than mammography. Overall the sensitivity of USG is more so, Ultrasound has long been used as an effective diagnostic tool in the evaluation of palpable and mammography abnormalities (14, 15, 16). Although ultrasonography, it is more sensitive than mammography in detecting lesions in women with dense breast tissue (14, 15, 16). In young women and women with dense breasts, ultrasound appears superior to mammography. Dense fibro glandular tissue is the most important inherent limitation of mammography in the diagnosis of breast cancer. Bilateral whole-breast US can be an effective adjunct imaging examination in the evaluation of women with dense breast tissue at mammography at cheaper expenses.

Tumor Size

Various studies have shown that the gross size of tumor is one of the most significant prognostic factors in breast carcinoma and there is increased incidence of axillary LN metastasis and decreased survival with increasing size of the tumor. In our study, most tumors were T2 (65%) at the time of diagnosis. These results show that in the large majority of our patients, the tumors were already of large size when women first sought medical help. This could be due to a lack of awareness among women and also because of an absence of screening protocol.

Majority of the tumors belonging to T2 and T3 were of grade 3(65% and 20% respectively) whereas only 6 of the T1 tumors were grade 1, suggesting that the larger tumors were more likely to be poorly differentiated and hence have a poor prognosis.

Histologic Type

In the present study, invasive ductal carcinoma, was the most common histologic type encountered, accounting for 92.5% of cases. Most invasive ductal carcinomas were grade 3; these tumors had cells showing minimal tubule formation, marked nuclear pleomorphism, and abundant mitoses.

Histologic Grade

Although histologic grade of breast cancer has been recognized for a long period of time, and its prognostic value has been validated in multiple independent studies, there are still some concerns regarding the incorporation of grade into the routine breast cancer staging systems.

However, a study by Boiesen et al, concerning inter-observer variation of histologic grade between seven pathology departments, have demonstrated a moderate degree of reproducibility.

Our study Nottingham Histologic Score system (the Elston-Ellis modification of Scarff-Bloom-Richardson grading system) was used. 47.5 % presented with grade 3 lesion. While 40 percent presented with grade 2 lesion.

Lymph Node Metastasis

A common first route of spread for breast carcinoma is through the axillary lymph nodes, and the incidence of ALNM increases with larger tumors. Nodal status is the most powerful independent prognostic factor in breast cancer and remains the most important feature for defining risk category. There is evidence that overall survival decreases as the number of positive nodes increases. Maximum 65 % patients were diagnosed with N1 stage. Our study shows higher the nodal stage the higher the grade of tumor.

Mammography

The Mammography reports collected. The BI- RADS classification used to grade. Only two grades were observed.Grade 4 suggested suspicious lesion while Grade 5 suggested confirmatory carcinoma. When mammography is compared with HPE (gold standard). 12.5 % cases showed grade 5 lesion suggesting confirmatory diagnosis.The sensitivity estimated the same. Specificity could not be commented as benign lesions were excluded from study.While sensitivity in more than 50 years of age was 20 %. As compared to 5 % in less than 50 years of age

USG

When USG is compared with HPE (gold standard) 17.5 % cases showed grade 5 lesion suggesting confirmatory diagnosis. The sensitivity estimated the same.Specificity could not be commented as benign lesions were excluded from study. While sensitivity in less than 50 years of age was 30 %. As compared to 5 % in more than 50 years of age

5. Conclusion

Our results indicate that breast density and age are important predictors of the accuracy of mammography. Breast ultrasound is more accurate than mammography in symptomatic women 50 years or younger, mammography has progressive improvement in sensitivity in women 50 years or older. The accuracy of mammograms increased as women's breasts became fattier and less dense. In young women and women with dense breasts, ultrasound appears superior to mammography, and may be an appropriate initial imaging test in those women.

Overall accuracy of USG is better than Mammography and it is cost friendly so can be used as screening of suspected Ca breast lesion routine basis.

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