

AN EVALUATION ON USING ULTRASOUND AS THE PRIMARY SCREENING TEST FOR BREAST CANCER

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Abstract

Introduction: Breast Cancer is a prevalent carcinoma with about 2.1 million new patients as recorded in 2018. Although mammography is the gold standard in detection of breast cancer but it is unavailable in many places due to several disadvantages. Instead, breast ultrasound has proved its worth in detecting palpable abnormalities of breast. The technique of ultrasound gains an upper hand due to its capability of detecting small nodules and the technique being affordable in regions with limited health screening devices.

Aims and Objectives: This study is intended to find out the efficacy of screening breast cancer by ultrasound and mammography and to find out the significance of ultrasound to be used as the primary screening method in breast cancer.

Materials and Methods: The study is of prospective design, conducted during the period of one year. The study has considered 70 patients. All the patients underwent both Mammography and Ultrasound, for 4 times. BI-RADS (Breast Imaging-Reporting and Data System) assessment scale was used for proper evaluation of the breast imaging.

Result: The significance test shows that there is no significant difference between screening ability of mammography and ultrasound which can strictly suggest not to replace mammography with ultrasound as the primary screening method ($P > 0.05$).

Conclusion: The study has concluded that the ultrasound can also be used as supplemental screening method where mammography is already available and ultrasound can be used as the primary screening method where mammography is not available or affordability is one of the issue.

Keywords: mammography, ultrasound, breast cancer, screening

Introduction

One of the major cause of Cancer related mortality among women is breast cancer around the globe. In 2018 alone about 2.1 million new patients suffering from breast cancer were reported [1]. Early detection and timely treatment are the twin pathways which when adopted in time can drastically reduce the mortality rate. The method of mammography is the gold standard in detection of breast cancer but this technique may not always be readily available particularly in limited resource settings. The reasons for the same can be varied ranging from high equipment cost to high maintenance cost (which includes both retention of skilled staff and radiologists for interpretation of result and up keep of the expensive instrument). Various studies have clearly indicated the scarcity of mammography units in third world Nations and South East Asia [2] as compared to West particularly US. In context of US where about 70% women can afford to undergo mammography very high percentage of overall sensitivity and specificity of digital mammography has been recorded [3,4]. Another effective means to detect breast cancer is breast ultrasound and its efficacy is enhanced because it is economic, can be easily applied in resource limited areas, and is applicable over a wide range of clinical manifestations. Breast ultrasound has proved its worth in

detecting palpable abnormalities of breast. It is equally effective in differentiating between cystic and solid masses and also provides useful information whether the solid mass (if found suspicious) needs a biopsy treatment [5-7]. Despite of the fact that incidences of breast cancer are much frequent in high income countries the mortality rates are very diminished as these areas are fully equipped with all available means of early detection and diagnosis [8,9]. Scarcity of data from lower income countries can lead to underestimation of disease burden from these areas [10]. This scenario turns worse when the exposed populace is ignorant of breast health causing delay in early detection [11]. The burden of breast cancer is augmenting with each passing decade as can be well explained from statistics obtained from China which reported 6.35 per 10000 mortality in the year 2014 [12]. But the fact that this scenario can be improved by effective screening of breast cancer cannot be ignored [13-15]. The most widely accepted screening program includes mammography however it cannot be uniformly (85% success) applied to all categories and sorts of women (dropping up to 47% in women with dense breast tissue) [16]; which has also been proven by previous studies [17]. The technique of ultrasound gains an

upper hand due to its capability of detecting small nodules and the technique being affordable in regions with limited health screening devices [18-20]. Thus the new cancer screening guidelines made a room for ultrasound stating that it can be regarded as an auxiliary screening method to mammography [21]. Metastasis status of axillary lymph node is an important parameter for determining decision regarding breast cancer [22]. Conventionally the status of the node used to be assessed by surgical methods like sentinel lymph node biopsy and axillary lymph node dissection the central biopsy method had very high efficiency rate and false negative were very rare but there were potential complications leading to over treatment associated with both above methods as they were surgical in nature. The ultrasound way of detection of breast cancer is gaining fast popularity because offers no invasive nature along with being radiation free real time and is highly tolerable in women. Earlier studies in this field have well prone that axillary ultrasound can provide meaningful information regarding axillary lymph node status in breast cancer patients [23]. But this method when taking alone exhibits only moderate sensibility and cannot be fully relied to conclude presence of nodal metastasis [24].

Materials and Methods

The study is of prospective design and was conducted during the period of one year. The study has included asymptomatic females who had been diagnosed with breast cancer (any type and at any stage) based on biopsy result, their age ranged between 26 years and 85 years at the beginning of the study, patients who gave consent for the study and who cooperated with the study process. The patients who attended the outpatient department of our hospital, were only included. The patients who are excluded were those who had other chronic conditions, uncooperative patients, those who dropped out of the treatment protocol. After applying inclusion and exclusion criteria, the study considered 70 patients. All the patients underwent both Mammography and Ultrasound, for 4 times. Those 4 points of screening were January, 2019 (Screening Point 1), February, 2020

(Screening Point 2), January, 2021 (Screening Point 3) and March, 2022 (Screening Point 4). For each patient, digital mammography was performed while ultrasound was performed by using high resolution transducer with frequency of 12 MHz. The radiologists who performed and interpreted with mammography and ultrasound were different persons. Even the results of the mammography and ultrasound was never shared between the doctors performing each of them. However, the radiologists were revealed the risk factors and other histories of each patient.

BI-RADS (Breast Imaging-Reporting and Data System) assessment scale was used for proper evaluation of the breast imaging. The study considered invasive or intraductal type of breast cancer to be the positive breast cancer.

Statistical analysis

The study considered SPSS 25 for data analysis. Sensitivity and Specificity were analyzed by McNemar's test. The sensitivity, specificity were determined and staging of the cancer was done. The level of significance was considered to be $\alpha = 0.05$.

Results

The study considered 70 patients for screening. The age of the whole study sample was 57.87 ± 16.73 years old. Out of 70 patients, 58 patients (82.85%) had invasive type. The study found that ultrasound has missed screening of 6 cases which is comparable to the missed screening by mammography. The significance test shows that there is no significant difference between screening ability of mammography and ultrasound which can strictly suggest not to replace mammography with ultrasound as the primary screening method ($P > 0.05$). The study has found the significance value of screening ability of mammography and ultrasound based on density of the lesion, age of the patients and stage of the carcinoma. Table 1 refers to the detailed findings in our study.

Table 1: The number of patients who were successfully screened by ultrasound, mammography and confirmed by biopsy and *p*-values of each comparable factor between ultrasound and mammography

Density	Screened with Ultrasound	Screened with Mammography	Biopsy result	* <i>P</i> -value (comparison of diagnostic efficiency between Ultrasound and Mammography)
< 25%	3	4	5	$P > 0.05$
26-50	4	5	6	$P > 0.05$
51-75	22	22	24	$P > 0.05$
76-90	23	23	23	$P > 0.05$
> 90	12	12	12	$P > 0.05$
Undetermined	6	4	0	$P > 0.05$
Age				
26-35	6	6	6	$P > 0.05$
36-45	24	25	26	$P > 0.05$
46-60	16	19	21	$P > 0.05$
60-75	13	15	17	$P > 0.05$

Stage				
0	18	19	22	P>0.05
I	21	22	23	P>0.05
IIA	12	12	12	P>0.05
IIB	6	6	6	P>0.05
IIIA	3	3	3	P>0.05
IIIB	2	2	2	P>0.05
IIIC	2	2	2	P>0.05
IV	0	0	0	

* $\alpha = 0.05$

The study further found that the ultrasound failed to screen lesion whose density is from minimum to 75% but lesions of higher density were screened successfully. Correlating with this finding, ultrasound failed to screen breast cancer of Stage 0 (in-situ) and stage I only. Higher staged carcinomas were efficiently screened by ultrasound. The sensitivity of screening breast cancer by ultrasound was found to be 91.42% while for mammography, it was found to be 94.28%, which is not appreciable difference.

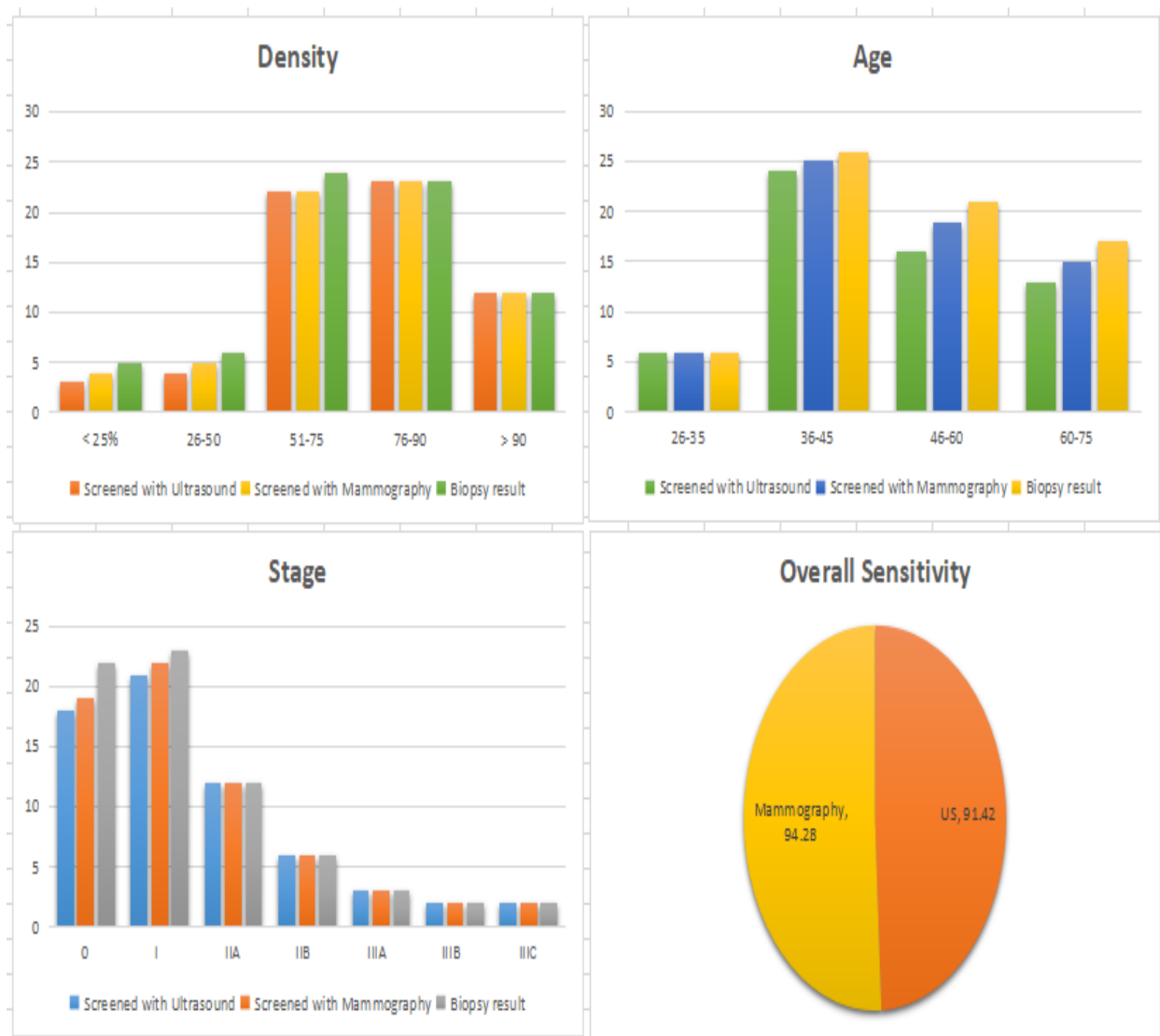


Figure 1: The number of patients screened by ultrasound, mammography and diagnosed by biopsy (Top left, top right, bottom left); The sensitivity percentage of mammography and ultrasound (bottom right).

Discussion

The most widely accepted technique for screening of breast cancers has always been mammography but in case of dense breasts its effectiveness is quite questionable. Ultrasound of breast has a merged as an effective auxiliary method in screening of breast cancer. This study had compared two types of ultrasound methods namely automated and handheld types. The study gave the detailed description of various kinds of handling and usage of automated breast ultrasound particularly mentioning about the artefacts and stating that these are different than those in handheld ultrasound devices [25]. There are various methods and techniques to detect breast cancer but they are complex, are subjected to human errors, and sometimes not absolutely appropriate. This study emphasized the use of many computer based interdisciplinary systems that can be deployed to minimize human errors and lead to a better diagnosis. More than 180 breast ultrasound images using multi-fractal dimensions and back propagation neural networks were studied for intricate details. The cases included 72 tumor cases and more than 110 normal cases. The results obtained exhibited around 80% success in precision, sensitivity, and specificity [26]. A very highly sensitive and accurate computer aided detection system CAD was applied to compare diagnostic accuracy and interpretation time of screening automatic breast ultrasound of women which had dense breast tissue. A comparative analysis was done once using the CAD system and other time without this system. The outcome exhibited that usage of concurrent-read CAD system was not only time saving but was very effective and resulted in non-inferior diagnostic accuracy while for screening of those women that had dense breast tissue and were asymptomatic [27]. Present study enlightened about the shortcomings of mammography in breast cancer detection despite of being a milestone in this field for decades. The presence of dense breasts further limits accuracy of mammography. Hence, the study laid emphasis on usage of ultrasound and magnetic resonance imaging laying particular emphasis on ultrasound so that occult breast cancer can be detected in the initial stages and subjected to early treatment [28]. The study laid emphasis on various methods of detecting cancer and stated that MRI is an expensive option because it always requires a contrast medium which may be hazardous for human health. Results from the study reveal that ultrasound is a better option which is relatively inexpensive and is devoid of any injected contrast or ionizing radiation; but it also states that its usage gets limited because it is time consuming and the hand scanning has its own limitations. The study thus recommends the usage of automated whole breast ultrasound which is quick and provides the radiologist a lot of images because he is not engaged in doing the scan. The study in particular emphasizes on two dimensional automated whole breast ultrasound that involves cine loop of axial images and the image spacing is <1 mm, which is subjected to high resolution monitor to detect any small lumps of cancer that might otherwise go unnoticed. The authors also claimed that a blinded study that combined the above technique with mammography results gave inputs that were two times better

in cancer detection and three times effective to detect cancer in dense breasts. The study accepted that mammography has been a very effective tool in detection of ductal carcinoma *in situ* [29]. Mammography which is a widely used tool in detection of breast cancer has its limitations which are well recognized and the need of the hour is switching over to other detecting devices. According to this study there can be of two types of screening including ultrasound and MRI. Authors opine that more than one screening tools should be applied in dubious cases and also the recommendations provided by renowned medical agencies should be followed as those recommendations are based on available evidence and in cases where evidence is insufficient the recommendations were based on cumulative opinion of the fellows and executive committee members which should be respected and kept in mind while deciding the case and the treatment [30]. There have been reported many incidences where automated breast ultrasound detected lumps of breast tissue which later turned out to be benign either in biopsy or on follow up. In this context this study targeted to find the impact of double reading automated breast ultrasound either with digital mammography or with digital breast tomosynthesis for accurately screening of breast cancer. More than 120 women participated with complete follow up having certain kind of breast cancer history (either individual or family related). Results from the study reveal that the combination therapy using either of the methods enhanced the recall rate; it was also observed that double reading when done during early phase was considerable to reduce false positive cases [31]. This population based breast cancer study was conducted in China and more than 70,000 women were included in the study. Results from the study reveal that near about 10,000 women tested positive for breast cancer by ultrasound screening and more than 8000 among them had BI-RADS category III, IV and V. Major regions that were identified by the study as being causative agents of breast cancer included young age, a highly matured age for first live birth, shorter span of breastfeeding etc. The results from the study were found satisfactory; the major limitation being that multivariate prediction model that was especially framed for this study gave only moderate prediction accuracy. Prediction Models were based on environment originated risk factors [21]. This study emphasized how important early detection of breast cancer can be in various age groups of women. The study recommends that annual mammographic should be performed on women after they attain the age of 40 and who fall in the average risk category. Those women who fall under high risk category should start their annual mammographic along with supplemented screening modalities as early as age of 30. MRI of breast region was also recommended particularly for those females who either had a personal history, had dense breasts, or were found to report breast lumps at around the age of 50. Ultrasound technique was chosen over MRI for those women who were not able to undergo MRI. The maximum age of 30 years was a set for women with ethnicity of either being black or belonging to Ashkenazi Jewish descendants [32]. To increase the efficiency of automated breast ultrasound this

study recommended the use of a computer aided diagnosis which was based on convolutional neural network (CNN) which was able to differentiate between breast lesions in two categories of benign and malignant. CNN depended on a modified Inception-v3 architecture that enabled efficient feature extraction in augmented breast ultrasound imaging. As this imaging provides pictures from two angles transfers and coronal it becomes more easy to have multiview of them. The high rate of success that was encountered in the study stated that CNN can be used as a second reviewer for expanding diagnostic reliability [33].

Conclusion

The study pointed out an essential point regarding the screening of the breast cancer. There are several disadvantages of mammography including high cost, high radiation exposure, requires space to install, requires Lead coated walls where it will be kept, etc [34]. Hence ultrasound, being much cost efficient and having other advantages as compared to mammography, can be used in the areas where mammography is not available. The study has revealed that ultrasound can be used to obtain a good analytically comparable result with that of mammography. This current study also suggests that there is a need to conduct more studies with larger population of different types and places. It can be considered that the ultrasound can also be used as supplemental screening method where mammography is already available and ultrasound can be used as the primary screening method where mammography is not available or affordability is one of the issue.

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