Original Article

Diagnostic Accuracy of Ultrasonography in the Diagnosis of Breast Carcinoma in Mammographically Dense Breasts: Histopathology as the Gold Standard

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Abstract

Objective: To evaluate the diagnostic accuracy of ultrasonography (US) in the diagnosis of breast cancer in women with mammographically dense breasts.

Methodology: This cross-sectional validation study was conducted at the Department of Radiology, PHQ Gilgit, from March 24th, 2021, to September 23rd, 2021, utilizing a non-probability consecutive sampling technique. A prospective study of 140 women with mammographically dense breasts (BIRADS 3 and 4) aged 25-60 years was conducted. All women underwent US and histopathology for the evaluation of breast lesions. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of US were compared to histopathology. SPSS version 24 was employed for data entry and analysis, calculating mean ± SD for quantitative data such as female age, and using frequency and percentage for categorical data like diagnosis on ultrasonography and histopathology.

Results: The sensitivity of US was 91.67%, the specificity was 83.93%, the PPV was 89.53%, the NPV was 87.04%, and the diagnostic accuracy was 88.57%.

Conclusion: US is a highly accurate modality for the diagnosis of breast cancer in women with mammographically dense breasts. It is a valuable tool for the early detection of breast cancer in these women.

Keywords: Breast cancer, ultrasonography, mammography, dense breasts, histopathology.

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Introduction

Breast cancer is the most common malignancy affecting women in many parts of theworld.[1] It is responsible for 21% of new cancer cases worldwide. It is also prevalent among women in Pakistan (accounting for one-third of the cancers in females).[2] In Pakistan among all carcinomas the rate of breast cancer is 19.33%.[3] The five-year survival of stage IV breast cancer is 10% while earlier detection and treatment can improve five-year survival to 85%.[2] Hence, the early detection has therefore, become necessary to reduce morbidity and mortality from the disease.[1]

Carcinoma Breast is regarded as one of the most common malignancies, accounting for 22% of all the cancers in the female population worldwide. Ultrasound guided (US) core biopsy is considered superior to surgical biopsy of suspicious breast lesion in terms of convenience, cost, and being less invasive. Most patients are reluctant to be subjected to biopsy as it is a painful and invasive procedure; and it has been concluded that 75% of these biopsies are proven to be benign in pathologic reports.[4-6] Therefore, combining reliability and minimally invasive approach is the need of

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the hour for such suspicious breast lesions.[7] It has been observed that imaging features on ultrasonography may be useful in differentiating benign from malignant breast masses and this can eventually decrease the need for diagnostic biopsies.[8] The criteria for differentiating between benign and malignant lesions from gray scale sonography are widely accepted.[9]

The accuracy of clinical diagnosis, mammography and breast ultrasonography in the preoperative assessment of breast cancer is necessary for early diagnosis. It is also to allow accurate pre-treatment planning to allow neoadjuvant chemotherapy or a single surgical intervention with clear surgical margins to reduce the incidence of tumor recurrence as patients usually abscond after the first surgical intervention.[1, 4]

Because of frequent overlap of radiologic signs breast lesions have to be biopsied to prove their malignancy or benignity.[5] With the introduction of BIRADS classification radiologist can define sonographic features and define final assessment category associated with the most appropriate management of the case. If these reliable criteria of sonographic BI-RADS classification are strictly followed the number of biopsies for benign lesions could be avoided.[5,6] Currently, the Breast Imaging and Reporting Data (BI-RADS) score of I to VI based on radiologists' subjective assessment is being reported, which is a coarse qualitative measure.[7]

In 2011 a study was done and they reported sensitivity of ultrasound as 92.1% and specificity of US as 80%.[8] In 2009 another study reported that sensitivity of US was 72.6% specificity of US was 73.9%. [9]

We find no local study in this subject and published international data approved role of ultrasonography in dense breasts.[8, 9] Mammography is known to be the best breast cancer screening test with a sensitivity of 85–95%; this test can help with the diagnosis of symptomatic or asymptomatic breast diseases. However, there are certain limitations to this technique such as the relatively high rate of false-negative mammograms. In women with dense breast tissue, the sensitivity of mammography is reduced to 47.8–64.4%.[10]

Furthermore, for a developing country like Pakistan where the facility of mammography is not easily available, ultrasound may be used as primary imaging modality because it inexpensive and readily available. In future females of local population who have mammographically dense breasts type 3 and 4 will be evaluated using ultrasonography and unnecessary biopsies could be avoided.

The aim of the study to assess the diagnostic accuracy of ultrasonography in diagnosis of breast cancer in mammographically dense breasts keeping histopathology as gold standard.

Methodology

This cross-sectional validation study was conducted at the Department of Radiology, PHQ hospital Gilgit, from March 24th, 2021, to September 23rd, 2021, utilizing a non-probability consecutive sampling technique. The sample size, estimated using a prevalence of breast cancer at 19.33%, specificity of ultrasound at 80%, and sensitivity of ultrasound at 91.1%, with margins of error of 10% and 9% respectively, was determined at a 95% confidence level.

Females aged 35 to 60 years with mammographically dense breasts categorized as 3 and 4 (per operational definition) were included. Exclusion criteria comprised confirmed pregnancy, lactating females, women with breast implants due to medical reasons, and those who had undergone whole breast ultrasound within the previous 11 months.

Data collection, performed by the researcher using a predefined Performa, commenced after approval of the synopsis. Informed consent was obtained from the 140 eligible females enrolled in the study. Demographic and clinical data were gathered from participants. To mitigate bias, a single consultant conducted all radiological investigations using a Voluson E6 ultrasound machine. Ultrasound examinations were conducted with patients in a supine position, and the lateral parts of the breast were investigated with the arms raised in a position of contralateral posterior oblique.

Histopathological examination, conducted by the hospital laboratory using True-cut biopsy, was compared with ultrasound reports via a 2 x 2 table. SPSS version 24 was employed for data entry and analysis, calculating mean ± SD for quantitative data such as female age, and using frequency and percentage for categorical data like diagnosis on ultrasonography and histopathology.

Diagnostic accuracy metrics (sensitivity, specificity, PPV, NPV, and overall diagnostic accuracy) of ultrasound were determined using histopathology as the gold standard. Stratification by female age was performed to address potential effect modifiers, with

post-stratified diagnostic accuracy calculated accordingly.

		Histopathology		Total
		Malignant	Benign	
US	Malignant	TP	FP	TP + FP
	Benign	FN	TN	FN + TN
Total		TP + FN	FP + TN	TP+FP+ FN + TN

Histopathological findings: Malignancy was labeled if abnormal cells with high mitotic activity found along with markedly enlarge nucleus with variable pleomorphism.

Findings on ultrasonography: Malignancy was labeled if lesions are found with poorly defined margin, micro-calcification and posterior acoustic enhancement.

3rd and 4th category mammographically dense breasts: The category 3 was defined if we find Heterogeneously dense (dense area is 50– 74% of total breast area) that may lower the sensitivity of mammography and category 4 was defined if extremely dense (dense area is >75% of total breast area) is found which could obscure a breast lesion.

True positive (TP): If malignancy is found on Ultrasound and is also found on histopathology.

True negative (TN): If malignancy is not found on Ultrasound nor found on histopathology.

False positive (FP): If malignancy is found on Ultrasound but not found on histopathology.

False negative (FN): If malignancy is not found on Ultrasound but it is found on histopathology.

Sensitivity: ability of US to correctly identify breast carcinoma.

Specificity: ability of US to correctly identify those not having breast carcinoma.

PPV: probability of true positive among all positives.

NPV: probability of true negative among all negative cases.

Results

A total Age range in this study was from 35-60 years with mean age of 49.08 ± 6.77 years. Majority of the patients 72 (51.43%) were between 51 to 60 years of age as shown in Table II.

All the patients were subjected to breast ultrasound. In 186 US positive patients, 77 (True Positive) had malignant breast lesions and 09 (False Positive) had benign on histopathology findings. Among, 54 US negative patients, 07 (False Negative) had malignant breast lesions on histopathology whereas 47 (True Negative) had benign lesions on histopathology as shown in Table III.

Table II: Distribution of patients according to Age.

Age (years)	No. of Patients	%
35-50	68	48.57
51-60	72	51.43
Total	140	100.0

Table III: Diagnostic accuracy of ultrasonography in diagnosis of breast cancer in mammographically dense breasts keeping histopathology as gold standard.

	Malignant on Histopathology	Benign on Histopathology	P-value
Malignant on US	77 **(TP)***	09 **(FP)*****	**0.0001**
Benign on US	07 **(FN)****	47 **(TN)********	

Sensitivity: 91.67%
Specificity: 83.93%
Positive Predictive Value (PPV): 89.53%
Negative Predictive Value (NPV): 87.04%
Diagnostic Accuracy: 88.57%

Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography in diagnosis of breast cancer in mammographically dense breasts keeping histopathology as gold standard was 91.67%, 83.93%, 89.53%, 87.04% and 88.57% respectively.

Stratification of diagnostic accuracy with respect to age groups is shown in Table IV & V.

Table IV: Stratification of diagnostic accuracy with respect to age 35-50 years. (n=68)

	Malignant on Histopathology	Benign on Histopathology	P-Value
Malignant on US	38 **(TP)**	06 **(FP)**	**0.001**
Benign on US	02 **(FN)**	22 **(TN)**	

Sensitivity: 95.0%
Specificity: 78.57%
Positive Predictive Value (PPV): 86.36%
Negative Predictive Value (NPV): 91.67%
Diagnostic Accuracy: 88.24%

Table V: Stratification of diagnostic accuracy with respect to age 51-60 years. (n=72)

	Malignant on Histopathology	Benign on Histopathology	P-Value
Malignant on US	39 **(TP)**	03 **(FP)**	**0.001**
Benign on US	05 **(FN)**	25 **(TN)**	

Sensitivity: 88.64%
Specificity: 89.29%
Positive Predictive Value (PPV): 92.86%
Negative Predictive Value (NPV): 83.33%
Diagnostic Accuracy: 88.89%

Discussion

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 incompletely 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.[10-13]

All the patients were subjected to breast ultrasound. In 186 US positive patients, 77 (True Positive) had malignant breast lesions and 09 (False Positive) had benign on histopathology findings. Among, 54 US negative patients, 07 (False Negative) had malignant breast lesions on histopathology whereas 47 (True Negative) had benign lesions on histopathology. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography in diagnosis of breast cancer in mammographically dense breasts keeping histopathology as gold standard was 91.67%, 83.93%, 89.53%, 87.04% and 88.57% respectively. In 2011 a study was done and they reported sensitivity of ultrasound as 92.1% and specificity of US as 80%.[8]In 2009 another study reported that sensitivity of US was 72.6% specificity of US was 73.9%.[9]

In a study, it has been observed that the specificity of US for the diagnosis of malignant lumps is 70.0%, sensitivity is 77.8% and accuracy is 75.7%.[16] Guyeret al[17] reports a sensitivity of 91.2% and a specificity of 97.2%. Leuchtet al[18] reports about an accuracy rate of 91% for carcinomas and 74% for benign lesions. Another study[14] showed that the sensitivity and specificity of ultrasound for the diagnosis of benign/malignant lesions were 93.9% and 86.5%, respectively, and its positive and negative predictive values were 86.9% and 93.8%, respectively. The accuracy of ultrasound for the diagnosis of breast cancer was assessed in the US.[15] The accuracy of ultrasound in the diagnosis of malignant lesions was estimated at 99%, that is, all palpable malignant lesions in the breast were detectable by ultrasound; however, ultrasound findings cannot be used to rule out malignancy given the probability of false-negative results.[15] In a study from Pakistan, the sensitivity and specificity of ultrasound for the diagnosis of breast cancer were estimated at 95.24% and 68.75%, respectively.[19]

A meta-analysis[20] was aimed to compare the diagnostic performance of contrast-enhanced ultrasound (CEUS), conventional ultrasound (US) combined with CEUS (US + CEUS) and US for distinguishing breast lesions. A total of 10 studies were included, of which 9 compared the diagnostic performance of CEUS and US, and 5 studies compared US + CEUS and US. In those comparing CEUS versus US, the pooled sensitivity was 0.93 (95% CI: 0.91–0.95) versus 0.87 (95% CI: 0.85–0.90) and pooled specificity was 0.86 (95% CI: 0.84–0.88) versus 0.72 (95% CI: 0.69–0.75). In studies comparing US + CEUS versus US, the pooled sensitivity was 0.94 (95% CI: 0.92–0.96) versus 0.87 (95% CI: 0.84–0.90) and pooled specificity was 0.86 (95% CI: 0.82–0.89) versus 0.80 (95% CI: 0.76–0.84). In terms of diagnosing breast malignancy, areas under the curve of the summary receiver operating characteristic (of both CEUS ($p = 0.003$) and US + CEUS ($p = 0.000$) were statistically higher than that of US. Both CEUS alone and US + CEUS had better diagnostic performance than US in differentiation of breast lesions, and US + CEUS also had low negative likelihood ratio.[20]

Ultrasound is introduced as an optimal technique for the diagnosis of breast diseases.[21,22] Also, a former study proposed advanced ultrasound techniques such as Doppler as a selective modality for imaging breast masses.[23] Breast ultrasound is effective for the diagnosis of patients who do not require biopsy. The risk of false positives is another limitation of ultrasound screening. Therefore, future studies are recommended to investigate the efficiency of ultrasound in groups at high-risk for breast cancer.

Conclusion

This study concluded that ultrasound is a highly sensitive and accurate modality for diagnosing malignant breast lesions in dense breast. So, we recommend that conventional ultrasound should be used as a primary screening tool for accurate pre-operative identification of breast lesions in these patients in order to reduce morbidity and mortality of these patients.

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