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Diagnostic Accuracy of Ultrasound in the Detection of Malignant Focal Solid Breast Lesions Taking Biopsy as a Gold Standard

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Abstract
Background: Now a day's breast cancer is one of the most common causes of deaths and the most malignant condition among women. Objective: To determine diagnostic accuracy of ultrasound in detection of malignant focal solid breast lesions taking biopsy as a gold standard. Material and methods: This Cross-sectional analytical study was conducted at the department of radiology and pathology of Life Line Hospital. Duration of the study was 9 months after the aproval of synopsis. Ultrasound system (Toshiba Xario) with linear transducer, frequency ranging 7 to 14 MHZ. All 78 participants were scanned while observing international standards of American institute of ultrasound in medicine (AIUM) guidelines for breast sonography. Results: Total 78 females with solid breast lesions were included in this study, out of them 28 (35.90%) were found in right while 50(64.10%) in left side. The distribution of breast lesions in Upper outer quadrant, Lower outer quadrant, Upper inner quadrant, and Lower inner quadrant were 50 (64.10%), 45 (57.49%), 13 (16.67%), 16 (20.51%) and 4 (51.13%) respectively. Mean of the depth to width D/W ration in malignant was 0.78±0.098 (0.42-0.93), while in benign was 0.52±0.141(0.35-0.85). there was a significant difference between the D/W ratio of benign and malignant solid breast lesion. The specificity, sensitivity, positive predictive value, negative predictive value, and diagnostic accuracy of ultrasound while taking histopathology as gold standard were 94.74%, 95.24%, 98.18%, 86.96%, and 94.87% respectively. Conclusion: Ultrasound can differentiate benign and malignant solid breast lesion to a great extent. With the application of this sonographic criteria in the cases of solid breast lesion before biopsy for histologic examination the number of unwanted biopsies will be reduced to a great extent.

Keywords: Solid Breast Lesion, Breast Cancer, Biopsy, Sonography, Noninvasive Method.

Introduction

Cancer is a dreadful condition that is characterized by uncontrollable growth of the cells in organ or from site from where cells are originating[1,2]. Cancer of the breast is most malignant condition of the breast and among women is the 2nd most common type of cancer.[3] Breast cancer starts to develop in the tissues of the breast or may begin in the lobes or ducts.[4] If the spread of the cancerous cell is not controlled timely, the division continuously takes place and ultimately results in the development of a lump or tumor.[5] The incidence rate of the breast cancer mortality in females is 20%.[6] It mostly affects the women more than 50years of age, but it can also find in young age too. The commonest site that is affected with the tumor is upper outer quadrant (60%).[7] The causes of the breast cancer include hormonal causes, when the cells come in contact with estrogen hormone or genetic factors like gene mutation.[8] The risk factors of breast cancer are as follows: start of menopause in late age of life, no breast feeding, women who deliver their 1st child in age of 30 years or above, having no children, women who have breast cancer in family history, use of contraceptive pills, being obese after menopause, smoking, alcohol or lack of exercise etc.[9] The following are the signs and symptoms of the breast: formation of the new lump in the breast or underarm, swelling or thickening of the affected part of breast, formation of the mass with hard or irregular borders, dimpling or irritation of the breast skin, appearance of skin flakes or redness in the breast or nipple area, pain in the nipple area, discharge from the nipple other than breast milk, change in the size and shape of the breast etc.[10] According to the classification of W.H.O the carcinoma of breast is invasive and no-invasive carcinoma.[11] Invasive carcinoma is further classified into invasive ductal carcinoma is the most commonly found carcinoma (80%), invasive lobular carcinoma is next to the invasive ductal carcinoma and found almost 10%, mucinous carcinoma seen in 2% population, medullary carcinoma in 5% of affected women, papillary carcinoma in 1%, tubular carcinoma in 1%, adenoid cyst carcinoma, apocrine carcinoma, secretory carcinoma, inflammatory carcinoma and metaplastic carcinoma.[11] Non-invasive carcinoma is further classified into ductal carcinoma in situ (DCIS) (25 – 70%), lobular carcinoma in situ (LCIS) (25 – 35%) and Paget's disease (1 -2%) of nipple (without any mass).[11] Ductal carcinoma in situ originates from the terminal duct lobular units. The patient will complaint of mass, pain and discharge.[12] They are mostly ipsilateral. Different types of ductal carcinoma of situ can be find including: papillary subtype, cribriform subtype, solid subtype, comedo subtype (Figure # 1).[12] Lobular carcinoma in situ starts to originate from the lobules, the milk-producing glands at the end of the breast ducts.[13] There are no significant clinical signs and symptoms of this type. And no microcalcifications are seen on the mammogram. They are mostly bilateral.[13] Paget's disease of nipple is a condition which resembles the eczema especially of the nipple and areola. Breast lump posterior to the areola with hyperplasia of all layers of the epidermis can be found in this type. Thickening of the epidermis can be sequenced by the ulceration of skin. Staging of the Paget's disease is divided into with mass or without mass with good prognosis because it is slow in growth and can be diagnosed early.[14] Although breast cancer could be diagnosed with histopathology but Ultrasound with the modern advancement in hardware and software has the potential give some clue regarding it. Most of the breast solid lesion are benign in nature but due to the fear of breast cancer there are numerous benign cases undergo unwanted invasive biopsy procedures. If the sonographic criteria is applied to the breast masses for its nature and initial differentiation is made, this way the number of unwanted biopsy procedures could be reduced.

Material and methods

This Cross-sectional analytical study was conducted at the department of radiology and pathology of Life Line Hospital. Duration of the study was 9 months after the aproval of synopsis. Ultrasound system (Toshiba Xario) with linear transducer, frequency ranging 7 to 14 MHZ. All 78 participants were scanned while observing international standards of American institute of ultrasound in medicine (AIUM) guidelines for breast sonography. Inclusion criteria was female patients age 16 years and above. Having symptoms in unilateral or bilateral breast like lump, Swelling, Nipple discharge, Redness and pain for four weeks. All the patients having breast mass with the request of ultrasound and biopsy. Patients with previous breast surgery and The patient who is already on medication for breast cancer were excluded.

Results

Out of 78 patients mean age was 51.4231, minimum was 19, maximum was 81 and std. deviation was 14.79515. Total 78 females with solid breast lesions were included in this study, out of them 28 (35.90%) were found in right while 50(64.10%) in left side. Quadrant-wise distribution of solid breast lesions was summarized in both the breasts as 50 (64.10%), 45 (57.49%), 13 (16.67%), 16 (20.51%) and 4 (51.13%) in Upper outer quadrant, Lower outer quadrant, Upper inner quadrant, Lower inner quadrant respectively. Margins of the masses were Speculated in 27 (34.62%), Irregular in 17 (21.79%), Angular in 10 (12.82%), Micro lobulated in 1 (1.28%), Well defined in 15 (19.23%), Smooth in 7 (8.97%), and Macro lobulated in 1 (1.28%). A diverse echo-pattern was observed in all the solid breast lesions, which is summarized as; hypoechoic in 55 (70.50%), hyperechoic in 20 (25.64%), isoechoic in 2 (2.56%) and heterogeneous in 1 (1.28%) of all the individuals. There was vascularity (blood flow) in 55 (70.51%) while in 23 (29.49%) there was no vascularity out of the total solid breast lesions. on Ultrasound 55 (70.05%) were malignant, while 23 (29.05%) were benign. On biopsy out of 78 patients, 57 (78.08%) were malignant and 21 (26.92%) were benign. Comparison of the mean and standard deviation was done with independent sample t-test. Mean of the depth to width D/W ration in malignant was 0.78±0.098 (0.42-0.93), while in benign was 0.52±0.141(0.35-0.85). there was a significant difference between the D/W ratio of benign and malignant solid breast lesion. It was also observed that there is a great variation in the D/W ratio of benign as compared to malignant 0.141 and 0.098 respectively. The specificity, sensitivity, positive predictive value, and negative predictive value of ultrasound findings was calculated with the help of two by two table against histopathology (biopsy). The sensitivity was 94.74% (85.63-98.19), the specificity was 95.24% (77.33-99.15), the positive predictive value98.18% (90.39-99.68), the negative predictive value86.96% (67.87-95.46), and the overall diagnostic accuracy94.87% (87.54-97.99).

Discussions

Solid, palpable breast lesion is one of the most common cause of female anxiety and fear, while assuming that could be malignant. After breast pain, pulpable solid breast masses is the second commonest clinical presentation. careful physical examination along with various investigations can pinpoint the differential and can classify these masses either benign, malignant or equivocal.[15]

There are several causes of solid breast masses ranging from physiologic changes due to age or variation in hormone during normal menstrual cycle or pregnancy to the memory gland infection and surrounding tissue. Some of the most common causes of pulpable breast lesion are listed as; mastitis (an infection in breast tissue that most commonly affects women who are breast-feeding), fibroadenoma, fibrocystic breasts (lumpy or rope-like breast tissue), breast cysts, injury or trauma to the breast, intraductal papilloma (a benign, wartlike growth in a milk duct), lipoma (a slow-growing, doughy mass that's usually harmless), milk cyst (galactocele) — a milk-filled cyst that's usually harmless, and breast cancer, etc.[16]

A study was conducted in Agha khan university hospital, Karachi in 2018 to determine the sonographic negative predictive value of the breast lesion, which are morphologically benign. It was also aimed to know whether follow up could be an alternative to histopathology. For this purpose, they included 40 consecutive patients having 157 breast lesions which were declared benign with the help of ultrasonography. Amongst them 17 underwent histopathology and the result confirmed them as benign. The rest of the 140 lesions were followed for 2-years. Some of the remaining regressed in size while others remain benign. It was concluded that the negative predictive valued of the ultrasound is almost hundred percent.[17] To determine the negative predictive value of ultrasound in the estimation of tumor-free margins while taking biopsy as the gold standard, a study was conducted in 2017. All the 47 conveniently included patients were evaluate 54 breast lesions. ultrasound was performed for the detection of lesion and tumor-free margins in malignant lesion. Post-excision ultrasound was performed for the evaluation of lesion whether visualized or absent with localizing needle in situ, lesion dimensions, depth measurement between the superior margin of the lesion and its edge. All the masses were present on post-excision scan, amongst them 51.85% were documented as malignant while 48.14% as benign. Ultrasound declared all specimens as tumor-free margins. But only 2 lesions had spiculated margins and were proven to be invasive lobular carcinoma on histopathology. Therefore, the negative predictive value of the specimen sonography for margin detection was 92.8%. It was concluded that ultrasound of the excised breast

tumor specimen is a simple and reliable technique for confirmation of the tumor-free margins in non-palpable breast lesions.[18] In the current study 78 patients were conveniently included. Side of breast involved in solid breast lesions, quadrant of breast involved in the development of breast lesions, margins of various breast lesions, echopattern of the breast masses, vascularity of the breast masses, overall ultrasound findings to differentiate benign from malignant, and histopathology results to diagnose either the lesion is benign or malignant in the breast. Moreover, the sensitivity, specificity, positive predictive value and negative predictive value of ultrasound were checked against the histopathologic diagnosis.Detection of malignant breast cancer from benign without painful surgical biopsy requires accurate predictions and reliable diagnostic modalities. The controversial findings of equivocal lesions assessment results in unnecessary core or open breast biopsy. To determine the reliabilities the ultrasound feature of solid breast lesion a study was conducted in Agha khan university hospital, Karachi by Murad M; et al. Sonographic criteria was evaluated for the differentiation of benign and malignant breast masses in 100 participants after performing the histologic examination. The sonographic criteria interpreted by 2 experts of ultrasound, without knowledge of clinical history or histologic examination results. Then the sonographic features were compared with histologic results to determine the reliability of the sonography in benign or malignant nature of nodules. The sonographic appearances most likely to characterize benign solid breast masses were; a round or oval shape, well circumscribed depth to width (D/W) ratio smaller than 0.71. But the sonographic features of solid malignant breast lesions included irregular shape, spiculated margins and width (D/W) ratio greater than 0.71. If these three most reliable criteria had been strictly applied by the sonologist to differentiate benign from malignant pulpable breast masses then the number of unwanted biopsies will dramatically reduce and the overall cancer biopsy yield would have increased. It was concluded that ultrasound features can help differentiate benign from malignant solid breast lesions. However, operator dependency and operator knowledge are utmost important because ultrasound is more subjective rather than to yield objective results. Interobserver variability is important should be observed and cross checked before deferring the biopsy of solid breast lesions.[19]

In another study total 180 patients were included with 132 benign and 48 malignant. The accuracy of ultrasound results of the three observers were compared with gold-standard histopathology which yielded a result of 95.7%, 84.3% and 91.4% respectively[88]. In the current all of the above including vascularity were taken as variables and individually were checked for the differentiation of benign and malignant breast masses. The mean of the depth to width (D/W) ratio was compared benign and malignant breast lesions and a significant difference was found between them. It was calculated as 0.78±0.098 and 0.52±0.141 in malignant and benign respectively, which agree with previous studies as shown in table 15 and graph 9. The p-value of levene's test was 0.037, which means there was significant difference between both the means.

Conclusion

Ultrasound can differentiate benign and malignant solid breast lesion to a great extent. With the application of this sonographic criteria in the cases of solid breast lesion before biopsy for histologic examination the number of unwanted biopsies will be reduced to a great extent.

Recommendations

The reliability study should be performed on a large sample size to acquire more precise results.
The electrographic strain value should also be evaluated against the histopathology and should be added as a parameter in the sonographic criteria for the differentiation of solid benign and malignant breast lesions.

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Table 1: Descriptive Statistics of Age

Age	N	Minimum	Maximum	Mean	Std. Deviation
Total	78	19.00	81.00	51.4231	14.79515

Table 2: Comparison of the "Depth to width" (D/W) ratio mean and standard deviation with independent sample t-test

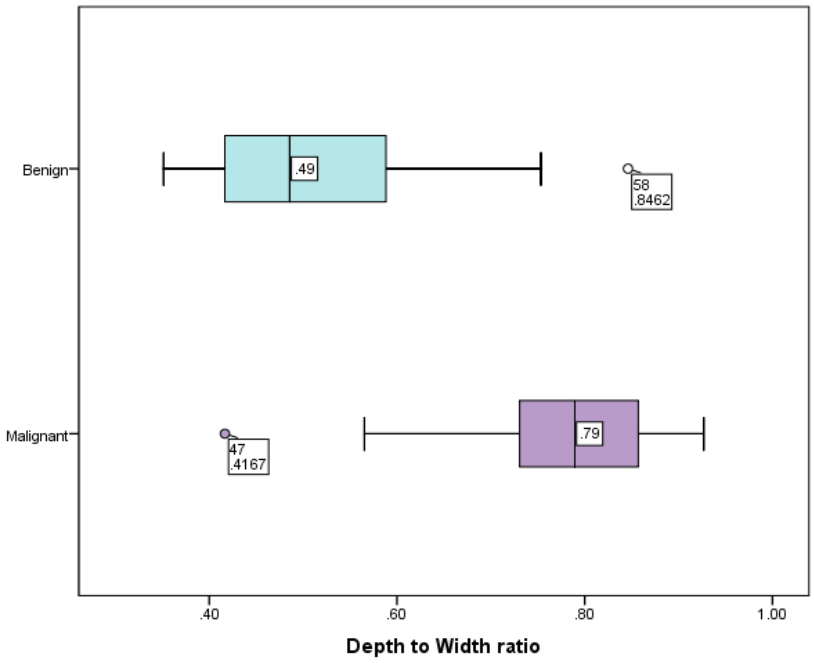
Group Statistics						
D/W Ratio	**Biopsy result**	**N**	**Mean**	**Std. Deviation**	**Minimum**	**Maximum**
	Malignant	57	0.78	0.098	0.42	0.93
	Benign	21	0.52	0.141	0.35	0.85
	Total	78	0.71	0.16	0.35	0.93

Table 3: Cross tabulation of ultrasound findings versus biopsy results with the help of two by two table to find our sensitivity, specificity, positive predictive value and negative predictive value

		Biopsy Findings			
		Malignant	**Benign**	**Total**	**P-value**
Ultrasound Findings	**Malignant**	54	1	55	0.00
	Benign	3	20	23	0.00
Total		57	21	78	0.00

Sensitivity = 94.74%
Specificity = 95.24%
Positive Predictive Value = 98.18%
Negative Predictive Value = 86.96%
Diagnostic Accuracy = 94.87%

Graph 1: Box-Plot for the comparison of mean of depth to width in benign and malignant cases



Figures

Figure 1: Well defined isoechoic solid lesion, with smooth margins, in the left breast at the upper outer quadrant, in retroarelora region, measures 1.07cm x 1.07cm, with no vascularity observed.

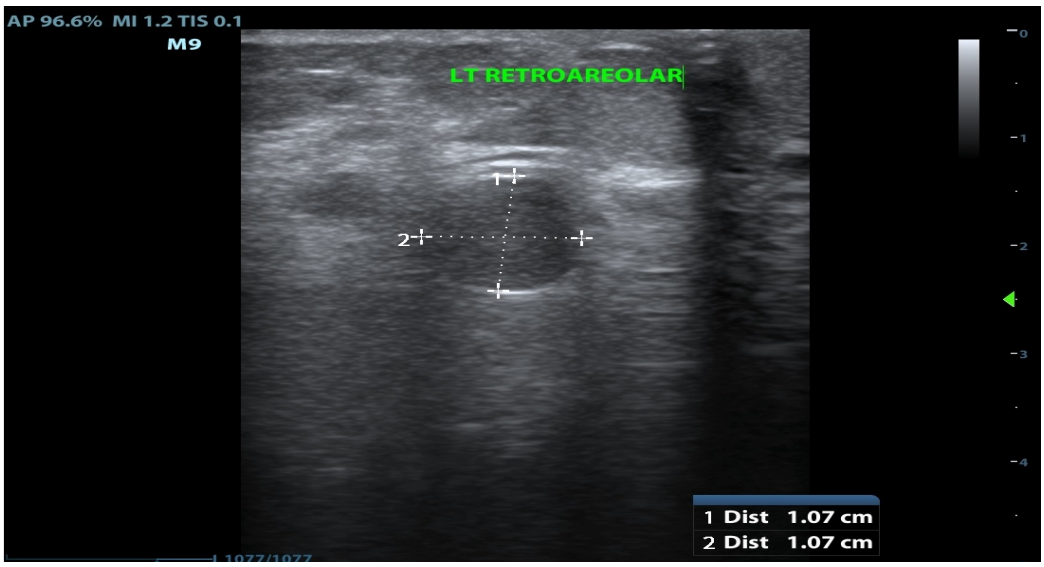


Figure II: Irregular hypoechoic solid lesion, in the left breast at the upper outer quadrant, measures 1.85cm x 1.27cm.