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Ultrasonographic Criteria of Breast Lesions: Radiologic-Histopathologic Correlation

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Abstract: ***This study aimed to utilize ultrasound features of breast lesions for characterization and differentiation between benign and malignant and correlate these criteria with histopathological findings.This is prospective hospital base study performed in the breast imaging facility at radiology department, at King Abdul-Aziz Specialist Hospital (KAASH), Taif city, Saudi Arabia during the period from Mar 2015 to Sep 2017 iincluded 200 female patients with 227 breast lesions who underwent ultrasound and ultrasound guided biopsy using a LOGIQ 7 unit (GE Healthcare) with a 12-MHz linear transducer, Core needle biopsy was performed by radiologists under ultrasound guidance using14-gauge Monopty® device (Bard, Tempe, AZ) with a 10-cm needle Suros 9-gauge vacuum-assisted CNB biopsy device (Hologic). Data analysed using SPSS version 20.The results of this study revealed that the mean age of the patients was 43 years ranged from 25-82 years. 227 indeterminate (Bi-RADS category 3) or suspicious breast lesions (Bi-RADS category 4 and 5) were found. Of these lesions, 71 were confirmed as malignant and 152 had benign histopathological features.US description of the lesions including mass shape, echo pattern, margin, boundary, orientation, posterior acoustic features, and calcifications as well as their power doppler flow criteria are demonstrated .Regarding the probability of malignancy, it was determined according to Bi-RADS for all lesions. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the grey scale US descriptors and power doppler criteria .Taking Bi-RADS category 4 as a cut point, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the lesions estimated Bi-RADS category as an indicator of malignancy. Then, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the lesions combining their Bi-RADS category and presence of penetrating vessels as indicators of malignancy. It concluded that Breast US is a useful diagnostic tool in breast cancer detection and can be used to characterize breast lesions. The vascular flow patterns of breast lesions on PDUS provide additional benefit for the differentiation of benign and malignant breast lesions.***

Keywords: Breast cancer, Breast US, Power Doppler US, US BI-RADS

1. Introduction

There are several types of tumours that may develop within different areas of the breast forming breast masses which are common in female. Most tumours are the result of benign (non-cancerous) changes within the breast while amongst all the breast masses, malignant masses are the most feared[1,2,3]. Breast cancer is the most common cause of cancer in women and the second most common cause of cancer death in women in the USA (United States of America).Breast cancer refers to cancers originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk[4].

Worldwide, breast cancer comprises (10.4%) of all cancer incidences among women, making it the second most common type of non-skin cancer (after lung cancer) and the fifth most common cause of cancer death. In 2004, breast cancer caused (519,000) deaths worldwide (7%) of cancer deaths; almost 1% of all deaths). Breast cancer is about 100 times more common in women than in men, although males tend to have poorer outcomes due to delays in diagnosis[4].

Saudi Arabia is no exception, where cancer of breast is most commonly prevalent. In one of the epidemiological studies conducted by Ravichandran et al[5], who reported that the incidence of breast cancer in Saudi Arabia was (19.8%) of all the female cancers detected in the Kingdom[6].

According to a report of Saudi National Cancer Registry (2000-2004), the incidence of breast cancer was 127.8per 100,000 women and the mortality rate was reported as 25.5 per 100,000[7]. A total of 7251 histologically confirmed new cases of cancer (4117 males and 3134 females) were seen in the 6-year period (1979 to 1984) in Riyadh[8].

In 1951 Wild and Reid[11], first developed equipment specially designed for breast scanning limited for differentiating between solid and cystic lesions, now, breast ultrasound proposes an attempt to characterize the breast ultrasound. The use of ultrasound in addition to clinical examination and mammography may result in an increased rate of breast cancer detection[9].

Breast ultrasound is of particular importance in those patients under 30 years of age as it is the usual initial breast imaging modality for them in many countries[10].

This is prospective hospital base study performed in the breast imaging facility at radiology department during the period from Mar 2015 to Sep 2017 at King Abdul-Aziz Specialist Hospital (KAASH), Taif city, Saudi Arabia. We retrospectively evaluated 200 female patients with 227 breast lesions who underwent ultrasound and ultrasound guided biopsy.

2. Materials and Methods

This is prospective hospital base study performed in the breast imaging facility at radiology department during the period from Mar 2015 to Sep 2017 at King Abdul-Aziz Specialist Hospital (KAASH), Taif city, Saudi Arabia.We retrospectively evaluated 200 female patients with 227 breast lesions who underwent ultrasound and ultrasound guided biopsy.

Imaging was acquired using a LOGIQ 7 unit (GE Healthcare) with a 12-MHz linear transducer.

All examinations were interpreted by one of three radiologists experienced in breast imaging. The radiologist described the site (clock position and distance from the nipple), size, imaging characteristics of the lesions, BI-RADS assessments, and management.

U/S features that used to characterize masses as benign were those showing: a round or oval shape, non-hypoechoic texture, circumscribed margins, parallel orientation, avascular/hypovascular with nodistal shadow and no calcifications (Figure, 1). Features that used to characterize masses as malignant included irregular shape, hypoechoic, microlobulated/angular/speculated margins(figure4), echogenic halo, non-parallel orientation(figure3), distal shadow, calcifications and penetrating vessels (figure2).

Core needle biopsy was performed by radiologists under ultrasound guidance using14-gauge Monopty® device (Bard, Tempe, AZ) with a 10-cm needle Suros 9-gauge vacuum-assisted CNB biopsy device (Hologic).

Lesions were classified into benign and malignant. Malignant lesions were classified into seven categories according to histology: 1-Invasive ductal carcinomas not otherwise specified, medullary, apocrine, neuroendocrine carcinoma;(figure5) 2- Tubular, mucinous, papillary carcinoma, cribriform carcinoma; 3- Metaplastic, anaplastic, undifferentiated high grade carcinoma;(figure6) 4- Invasive lobular carcinoma; 5- Mixed ductal and lobular carcinoma(figure7); 6- In situ carcinoma; and 7-metastatic carcinoma.

Statistical analysis

Data coded, entered and analysed using SPSS version 20. Descriptive statistical analysis was used to determine frequency distribution to obtained demographic variables in tables and graphs .

Ethical considerations

- Research proposal was approved from Ethical Committee in Radiology department, (KAASH).
- There is no risk for study subjects during application of research. Ethical committee in (KAASH) was assured that the data of this research will not be reused without second permission
- Official permission to conduct the study was obtained from the research committee in King Abdul-Aziz Specialist Hospital (KAASH).

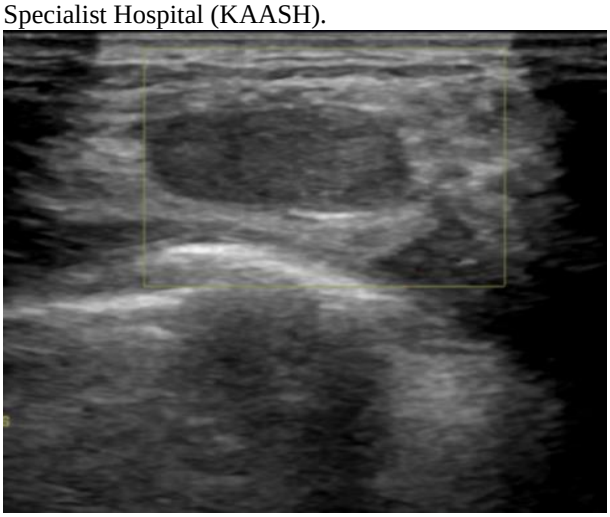


Figure 1: Doppler US image shows no penetrating vessels in an oval hyperechoic mass with regular margins and parallel orientation. No microcalcifications or distal shadow.

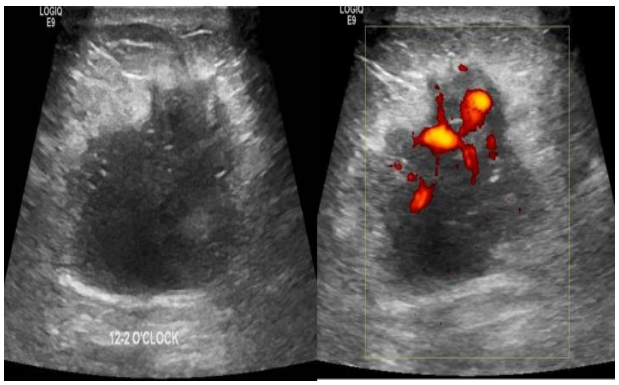


Figure 2: Grey scale and Power Doppler US image shows penetrating vessels in an irregular hypoechoic mass with microcalcifications and angular margins. The vessels are seen coursing into the mass.

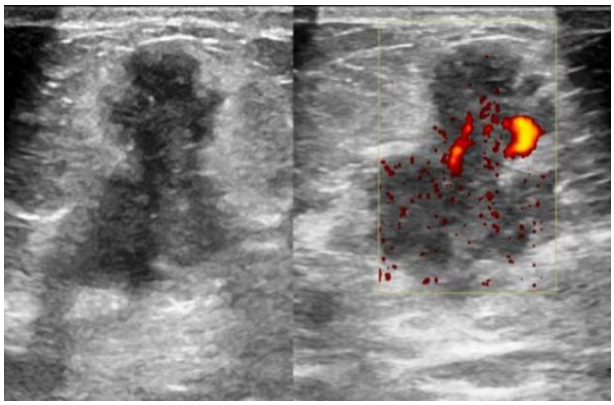


Figure 3: Grey scale and Power Doppler US image shows penetrating vessels in an irregular hypoechoic mass with microcalcifications, angular/mocrolobulated margins and non-parallel orientation.

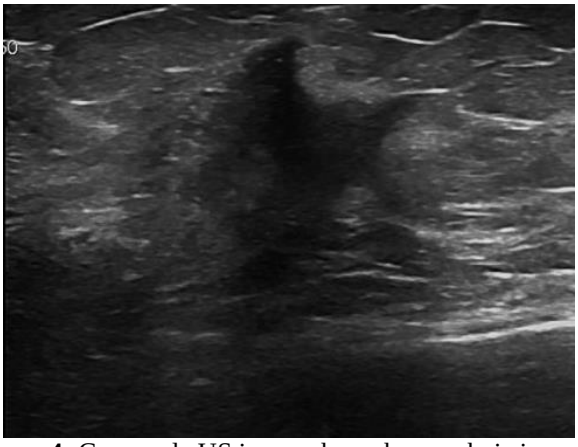


Figure 4: Grey scale US image shows hypo echoic irregular with speculated margins, non-parallel orientation and distal shadow.

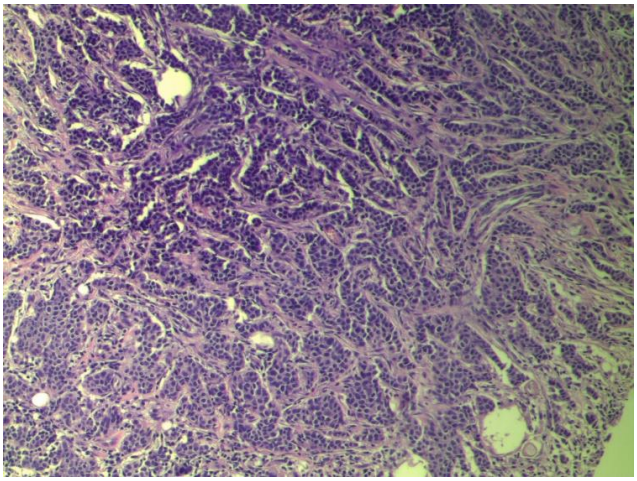
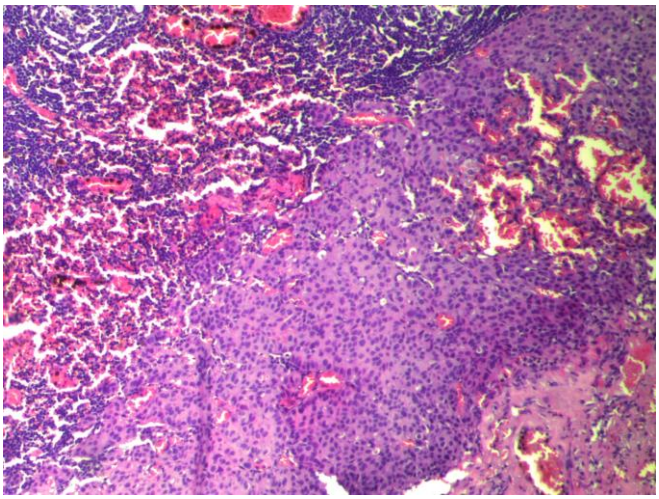


Figure (5): Breast mass diagnosed as invasive duct carcinoma grade II (TRU-CUT BIOPSY)



Figure(6): Metastasic Carcinoma to Axillary Lymph Node (Arrow).

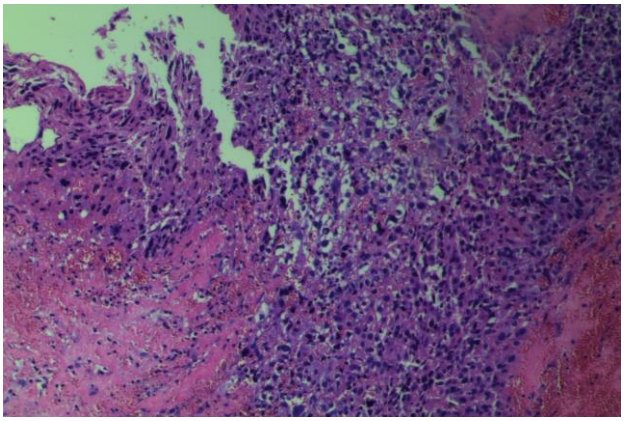


Figure (7): Breast mass by U/S It was A Complex cystic mass Histopathology Diagnosis was invasive mammary carcinoma

3. Results

The mean age of the 200 patients was 43 years (ranging from 25-82 years). 227 indeterminate (Bi-RADS category 3) or suspicious breast lesions (Bi-RADS category 4 and 5) were found. Of these lesions, 71 were confirmed to be malignant (Table 1) and 152 had benign histopathological features (Table 2).US description of the lesions including mass shape, echo pattern, margin, boundary, orientation, posterior acoustic features, and calcifications as well as their power doppler flow criteria (penetrating vessels) are demonstrated in Table 3.

Regarding the probability of malignancy, it was determined by the radiologists according to Bi-RADS for all lesions (Table 4).The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the greyscale US descriptors and power doppler criteria (penetrating vessels) (Tables 5 & 6).

Table 1: Frequency distribution of histopathological patterns of the malignant breast lesions

Type of the lesion	Number of lesions	Percentage
Invasive ductal carcinoma	48	64.8
Ductal carcinoma in situ	4	5.4
Invasive lobular carcinoma	10	13.5
Lobular carcinoma in situ	2	2.7
Mixed invasive ductal and lobular carcinoma	1	1.4
Tubular carcinoma	1	1.4
Mucinous carcinoma	2	2.7
Undifferentiated carcinoma	3	4
Inflammatory carcinoma	2	2.7
Malignant Phyllodes tumor.	1	1.4
Total	74	100

Table 2: Frequency distribution of histopathological patterns of the benign breast lesions

Type of the lesion	Number of lesions	Percentage
Fibroadenoma	64	41.8
Fibrocystic disease	49	32
Fibroadenoma with fibrocystic disease	16	10.4
Non-specific mastitis with breast abscess	5	3.3
Granulomatous mastitis	3	2
Tuberculosis mastitis	3	2
Lactating adenoma	2	1.3
Breast abscess	2	1.3
Duct papilloma	2	1.3
Benign phyllodes	2	1.3
Lipoma	1	0.7
Fat necrosis	4	2.6
Total	153	100

Table 3: Frequency of Benign and Malignant Masses for grey scale US Descriptors and Power doppler flow criteria

US Descriptor	Nu	A	Benign	B	Malignant	C
Shape						
Oval	127	56	117	92	10	8
Round	11	5	9	82	2	18
Irregular	89	39	27	30	62	70
Echogenicity						
Non-hypoechoic	84	37	33	39	51	61
Hypoechoic	143	63	89	62	54	38
Margin						
Circumscribed	110	48	101	92	9	8
Indistinct	54	24	29	54	25	46
Angular	25	11	10	40	15	60
Microlobulated	29	13	12	41	17	59
Speculated	9	4	1	11	8	89
Boundary						
Abrupt interface	155	68	61	39	94	61
Echogenic halo	74	32	46	62	28	38
Orientation						
Parallel	170	75	134	79	36	21
Not parallel	57	25	19	33	38	67
Posterior acoustic features						
Normal	93	41	81	87	12	13
Enhancement	44	19	36	82	8	18
Shadowing	77	34	30	39	47	61
Mixed	13	6	6	46	7	54
Microcalcifications						
No	199	88	150	75	49	25
Yes	28	12	3	11	25	89
Power doppler flow criteria (penetrating vessels)						
No	181	80	141	78	40	22
Yes	46	20	12	26	34	74

A. percentage of 227 masses, B. percentage of benign lesions among total number of masses with given descriptor and C. Percentage of malignant lesions among total number of masses with given descriptor. Taking Bi-RADS category 4 as a cut point, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the lesions estimated Bi-RADS category as an indicator of malignancy (Table 7).Then, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the lesions combining their Bi-RADS category and presence of penetrating vessels as indicators of malignancy (Table 8).

Table 4: Number and incidence of malignant histological findings according to category of breast US findings in comparison to likelihood of malignancy of breast imaging reporting and data system (BI-RADS) categories for ultrasound

Category	Number of lesions	Percent of 223 lesions	Number of malignant lesions at histological examination	%	Expected rate of malignancy after US BI-RADS categorization (%)
3	15	6.7	0	0	< 2
4	139	61.5	5	3.6	3–94
5	73	31.8	69	94.5	> 94
Total	227	100	74	100	

Table 5: Statistical analysis of grey scale US descriptors and power doppler flow criteria for malignant lesions

Us descriptors	Sensitivity	Specificity	PPV	NPV
Irregular shape	83.8	82.4	69.7	91.3
Angular/speculated/ Microlobularmargins	81.6	81.5	63.5	91.8
Hypoechoic	51.4	27	37.8	39.3
Echogenic halo interface	23	57	37.8	39.4
Non-Parallel orientation	51.4	87.6	66.7	78.8
Distal shadow	70.1	79.6	61	85.4
Calcification	33.8	98	89.3	75.4
Penetrating vessels	45.9	92.2	73.9	77.9

Table 6: Statistical analysis of grey scale US descriptors and power doppler flow criteria for benign lesions

Us descriptors	Sensitivity	Specificity	PPV	NPV
Round or oval shape	82.4	83.8	91.3	69.7
Circumscribed margins	81.5	81.6	91.8	63.5
Non-hypoechoic	27	51.4	39.3	37.8
Abrupt interface	57	23	39.4	37.8
Parallel orientation	87.6	51.4	78.8	66.7
Distal shadow	79.6	70.1	85.4	61
Calcification	98	33.8	75.4	89.3
Penetrating vessels	92.2	45.9	77.9	73.9

Table 7: Statistical analysis of the lesions estimated Bi-RADS category as an indicator of malignancy

Category	Sensitivity	Specificity	PPV	NPV
4	100	10	3.6	100
5	100	78.9	94.5	100
4 and 5	100	10	35	100

Table 8: Statistical analysis of combined lesions estimated Bi-RADS category and presence of penetrating vessels as indicators of malignancy

Category	Sensitivity	Specificity	PPV	NPV
4+ Penetrating vessels	49.4	51.7	21	79.6
5+ Penetrating vessels	72	90.6	86.6	79.6
4 and 5+ Penetrating vessels	73	51	41.9	79.6

4. Discussion

US is an established, diagnostic tool that has been used to evaluate specific areas of abnormality discovered on either a clinical examination or mammography in order to characterize breast lesions and to differentiate between benign and malignant lesions[11,12].

In the present study, most of the lesions were suspicious or highly suspicious of malignancy (exhibiting one or more suspicious sonographic features) except for 15 lesions were not suspicious but biopsied standards being either in a patient with past history of cancer breast or larger than 2.5 cm diameter when first diagnosed or for patient psychological and mental relief.

Following Heinig J et al, Rahbar et al, Hong AS et al and Andrea S et al,[13-16] ,we used these U/S features to characterize masses as malignant: irregular shape, hypoechoic, microlobulated / angular / spiculated margins, echogenic halo, non-parallel orientation, distal shadow, calcifications and penetrating vessels. U/S features that used to characterize masses as benign were: round or oval shape, circumscribed margins, non-hypoechoic, abrupt interface, parallel orientation, with no distal shadow, no calcification and no penetrating vessels.

We did not include lesions with indistinct margin (29 benign and 25 malignant) and those with mixed posterior acoustic features (6 benign and 7 malignant) as both did not show significant difference between benign and malignant lesions.

In the present study finding US grey scale descriptors of shape, margin, orientation, posterior acoustic features and calcification can be used to predict whether the lesions were benign or malignant while echogenicity and boundary didn't show significant role.

This was concluded from high PPV for malignancy for irregular shape, microlobulated /angular/spiculated margins, non-parallel orientation, distal shadow and presence of calcifications (69.7, 63.5, 66.7, 61 and 89.3 respectively) and relatively low PPV for malignancy for low echogenicity and presence of echogenic halo (37.8 for both). For benign lesions these sonographic BI-RADS descriptors had a high predictively; round or oval shape, circumscribed margins, parallel orientation, no distal shadow and no calcification (91.3, 91.8, 78.8, 85.4 and 75.4 respectively) and relatively low PPV for benignity for non-hypochogenicity and presence abrupt interface (39.3 and 39.4 respectively).

These findings was comparable to those of Hong AS et al [33], who founded high predictive value for malignancy include spiculated margin (86%), irregular shape (62%), and nonparallel orientation (69%). While for sonographic BI-RADS descriptors with highly predictive of benign lesions included circumscribed margin (90%), parallel orientation (78%), and oval shape (84%).

Our findings also agreed with Rahbar et al [14], as they found US features that most reliably characterize masses as benign were a round or oval shape (94%), circumscribed margins (91%), and a wider then tall (89%). They also found features that characterize masses as malignant included irregular shape (61), microlobulated (67%) or spiculated (67%) margins, and taller than wide (40%).

But we disagree with Heinig J et al[13], regarding lesion orientation as they did not find the non-parallel orientation feature to be significantly associated with malignancy in contrast to Gokalp et al[17], and Stavros AT et al [18], who stated that non parallel orientation shown to correlate well with malignancy while parallel orientation is associated with benignity. They relied this to small sample size of their study or the size of the lesions examined, which were mostly > 2 cm.

Regarding penetrating vessels, we found a significant difference between malignant and benign lesions as presence of penetrating vessels had a high PPV, 73.9 for malignancy while their absence had a high PPV, 77.9 for benignity.

Our findings was comparable to those described by Raza and Baum[19], who found that the sensitivity, specificity, PPV and NPV of using penetrating vessels to predict malignancy were 68%, 95%, 85% and 88%, respectively.

Such findings are confirmed also by Studies conducted by Gokalp et al[35], Kwak et al [20], Lee et al [21] and later by [12], who found vascular patterns of the lesions, as seen on PDUS, correlated with the histopathology results in their study, with high specificity and NPV.

However, in the study of Ozdemir et al[22], neither morphologic nor spectral Doppler analysis proved to be successful on its own, but the information obtained could increase the diagnostic certainty of grayscale ultrasound and mammography[22]. Similar results were obtained in the study by Buadu et al[23] who concluded that even the combination of color and spectral Doppler analysis does not appear to contribute significantly to the differentiation between benign and malignant breast lesions[23].

For BI-RADS category correlation with malignancy, ACR indicates malignancy rates should be less than 2% in BI-RADS 3 lesions. In this study, none of the BI-RADS 3 lesions were defined as malignant (with an NPV of 100%), US sensitivity was 100 for both BI-RADS category 4 and 5 while false-positive rates were 96.4% for BI-RADS category 4, 5.5 % for BI-RADS category 5 and 65 % for combined BI-RADS category 4 and 5.

These results agreed with previous prospective clinical studies have evaluated the role of US in evaluation of breast masses[38-41], using BI-RADS category 4 as a cut-off point, the average sensitivities of US were > 95% (US range, 97.3-100%), whereas the average false-positive rates of US were approximately 60% (range, 56.8-68.2%).

Sensitivity and NPVs in our study (100% and 100%) were similar to Zengin B et al[42] and Graf et al[24] and little better when compared to other studies. Park et al[25] reported

a sensitivity of 96-100%, and NPV of 95-100% in their study. In a study conducted by Lee et al[26], sensitivity was reported as 97-98% and NPV as 94-96%. Constantini et al [27] reported their sensitivity was 98.2% and NPV was 95.2% in the study. In their study, Stavroset al[18] reported a sensitivity of 98.4% and NPV of 99.5%. Lai et al[46] reported a lower degree of sensivity and NPV as 91-95% and 81-93%, respectively.

Although the false positive results were high in our study, there are several studies in the literature in accordance with our findings. Zengin B et al[42] had (20.7% and 30.3) specificity results, Park et al[42] reported their specificity results ranged between 8 and 43%. This level was 26-40% in the study of Lee et al[26] and 45-77% in the study of Lai et al[28].

In our study, PPVs was 35%. This parameter was found to be ranging between 24.7 and 27.2% in Zengin B et al study[42], and to be 30-40%; 38%; and 72% in the studies of Stavros et al[18]; Park et al[43]; and Constantini et al[27], respectively.

In our study, PPVs was 3.6% for BI-RADS 4 lesions. These results are comparable with ACR statement of malignancy probability of BI-RADS 4 lesions as between 3-94%. However our results are lower than those of Yoon et al[29], Heining et al[13], Raza et al[43], and Wiratkapun et al[31] studies who reported PPVs of 18.6%, 17%, 16.2%, 21% respectively.

This could be explained by increased PPV with increased prevalence of malignancy and in our study, we encountered lower malignancy rate, 32.6% compared to higher malignancy rates of studies reported higher PPV results as it was 51.3%, 57.5%, and 53.3% in the studies of Lee et al[26], Constantini et al[27], and Lai et al[28], respectively.

In this study, PPVs was 94.5% for BI-RADS 5 lesions. These results are comparable with ACR statement of malignancy probability of BI-RADS 5 lesions as over 95%. It is also comparable with many studies presented rates for PPV of BI-RADS 5 lesions, ranging between 80 and 97% [24,26,27,30,32,33,34,35]. However other studies reported PPV of BI-RADS 5 lesions lower than stated by ACR, like Tan et al[36] (84%), Zengin B et al[42] (66.7-84.6%), Raza et al[30] (88.8%) and Hamy et al[37] (78.7%). Except Tan et al[36], the other studies who reported PPV of BI-RADS 5 lesions lower than stated by ACR, were conducted on non-palpable breast masses, so this might be one of the reasons for the lower rates in these studies.

Combining both grey scale US and PDUS method, we obtained a much higher diagnostic accuracy of PPV and specificity for combined BI-RADS 4 category and PDUS method (21% and 51.7%) than that obtained by BI-RADS 4 category alone (3.6% and 10%).

Also, there was higher diagnostic accuracy of PPV and specificity for combined BI-RADS 4,5 categories and PDUS method (41.9% and 51%) than that obtained by BI-RADS 4,5 categories alone (35% and 10%).

In the same time, diagnostic accuracy of PPV and specificity for combined BI-RADS 5 category and PDUS method (86.6% and 90.6%) were comparable with that obtained by BI-RADS 5 category alone (94.5% and 78.9%).

Regarding this point we agree with that reported by Kwak et al[20], Gokalp et al[35] and Ibrahim R et al[11].

The main problem of ultrasound is the dependence on different variables and being operator dependent. In this study 5 lesions were not seen in US initially, after revising mammography images, they were detected in the second look US of a particular area of the breast detected by mammography.

5. Conclusion

Breast US is a useful diagnostic tool in breast cancer detection and can be used to characterize breast lesions. The vascular flow patterns of breast lesions on PDUS provide additional benefit for the differentiation of benign and malignant breast lesions.

ACR BI-RADS lexicon provides standardized terminology to facilitate accurate and consistent breast sonography reporting and can be helpful in distinguishing benign from malignant breast masses.

Utilizing technologic advances can eliminate operator dependence-related mistakes.

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