



Value of Ultrasound in the Detection of Benign and Malignant Breast Diseases: A Diagnostic Accuracy Study

Farideh Gharekhanloo^{1*}, Mostafa Morad Haseli² and Saadat Torabian¹

¹Department of Radiology, Hamadan University of Medical Sciences, Hamadan, Iran

²Department of Social Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

ARTICLE INFO

Article history:

Received: 10 December 2017

Accepted: 7 April 2018

Online:

DOI 10.5001/omj.2018.71

Keywords:

Breast Diseases; Sensitivity and Specificity; Ultrasound; Breast Cancer.

ABSTRACT

Objectives: We sought to determine the diagnostic accuracy of ultrasound for benign and malignant breast lesions. **Methods:** This retrospective study was performed to evaluate the diagnostic accuracy of ultrasound in 203 patients with complete medical records who visited Mehr Medical Imaging Center for breast ultrasound between March 2014 and February 2016. The collected data comprised of demographic characteristics, ultrasound results (consisting of the anatomic area of the lesion, the involved side, and the ultrasound characteristics of the lesion), mammogram results, and pathology reports (if surgery or biopsy was performed). **Results:** For the diagnosis of malignant and benign lesions, ultrasound had a sensitivity of 93.9% and specificity of 86.5%; its positive and negative predictive values were 86.9% and 93.8%, respectively. Lesion type was significantly associated with a family history of breast cancer and fertility status ($p < 0.005$), but there was no significant association between the involved side and tumor type ($p > 0.050$). **Conclusions:** Mammography is the best technique for screening and identifying patients with non-mass-like breast lesions and microcalcifications. Considering the false positive and false-negative results, ultrasound is not a perfect screening modality. Future studies are recommended to study the value of ultrasound in the detection of high-risk breast cancer patients.

Breast diseases, classified as disorders of the reproductive system, are the most common problems among women. Breast masses are usually benign, and if diagnosed early, can be treated successfully.¹ In the Middle East, statistics show that breast cancer is the most common malignancy among the female population. In Iran, like other developing countries, the prevalence of breast cancer is a growing trend, accounting for 21.4% of all malignancies in Iranian women.²

Since breast cancer is the leading cause of mortality among the female population, identifying an accurate diagnostic tool to effectively manage this disease is critical.¹ 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.³ However, there are certain limitations to this technique such as the relatively high rate of false-negative mammograms. In addition, dense breast tissues, which are usually detected in about half of women under the age of 50 and one-third

of older women, can undermine the sensitivity of mammography. The accurate description of lesion components is essential due to the importance of distinguishing between benign and malignant masses. Further, non-invasive imaging techniques such as magnetic resonance imaging and ultrasound are used as auxiliary techniques.³ Therefore, identifying the most accurate diagnostic tools for breast diseases is necessary.⁴

Although the use of biopsy or fine-needle aspiration cytology is necessary to obtain accurate results, in patients with benign lesions, the mass tissue is recommended to remain intact.^{3,5} False-negative mammographic findings are reported in 4–12% of patients with palpable breast masses, suggesting the possibility of a malignant mass. Under such conditions, the treatment process is continued along with aspiration or biopsy of the suspected clinical lesions.⁶

Even though ultrasound is not considered a screening test, it can be employed as a supplementary technique in conjunction with mammography for the diagnosis of palpable masses. Ultrasound can

aid in the diagnosis of some cysts and lesions that are indistinguishable in mammography due to fibroglandular tissues surrounding them.⁶ The use of biopsy for the diagnosis of benign breast lesions is a serious issue as it leads to problems including fear of continuing treatment and repeating biopsy. In this regard, the use of ultrasound can eliminate unnecessary biopsies.⁷

Although ultrasound was initially used for determining the cystic nature of a mass, its role has become more prominent in recent years. Considering the absence of ionized rays in this technique, it can be applied as a low-risk technique in pregnant and lactating patients. Moreover, ultrasound can be utilized for patient's susceptible to inflammation caused by compression mammogram.⁸ On the other hand, the use of this diagnostic technique is strongly dependent on the radiologist's knowledge and expertise. Therefore, there is a high possibility of different interpretations and diagnoses in this technique. In this study, we aimed to determine the diagnostic accuracy of ultrasound in the detection of benign and malignant breast tumors in women who had visited Mehr Radiology Clinic between 2014 and 2016.

METHODS

In this retrospective study, we investigated the diagnostic accuracy of ultrasound using the medical records of patients who visited the Mehr Radiology Clinic of Hamadan University of Medical Sciences for radiological examination of the breast between March 2014 and February 2016. The participants were chosen through the convenience sampling method, and the sample size was calculated by using the following formula:

$$\text{Sample size} = \frac{(z_{\alpha} + z_{1-\beta})^2 \times (P_1q_1 + P_2q_2)}{(P_1 - P_2)^2}$$

$$N = \frac{(1/96 + 1/28)^2 \times (0/685 \times 343) + (0/451 \times 0/549)}{(0/658 - 0/452)^2} = 115$$

The medical records of 115 patients were used, which included demographic data, reasons for patient visit, family history of breast diseases, lactation history, duration of oral contraceptive pill (OCP) use, contact details of the patients, ultrasound findings including the anatomical position of the lesion, mammogram results (if present), and pathology reports (in case of surgery or biopsy).

Table 1: Demographic data and frequency of the patients based on the lesion characteristics observed in ultrasound reports.

Variables	Characteristics	Number (%), N = 203
Type of tumor	Benign	104 (51.2)
	Malignant	99 (48.8)
Axillary adenopathy	Yes	99 (48.8)
	No	104 (51.2)
Fertility status	Fertility	62 (30.5)
	Menopause	141 (69.5)
Tumoral	Yes	107 (52.7)
	No	96 (47.3)
Adenopathy	Yes	108 (53.2)
	No	94 (46.3)
Duration of lactation, months	0-4	115 (56.7)
	4-8	44 (21.7)
	8-12	19 (9.4)
	> 12	7 (3.4)
Duration of oral contraceptive pills use, months	< 12	131 (64.5)
	12-36	34 (16.7)
	36-62	17 (8.4)
	> 62	21 (10.3)
Mass size, cm	0-1	18 (8.9)
	1-2	52 (25.6)
	2-3	62 (34.5)
	3-4	30 (14.8)
	4-5	8 (3.9)
	5-6	6 (3.0)
	6-7	1 (0.5)
	7-8	2 (1.0)
Characteristics of lesions observed in ultrasound	Mild fibrocystic breast changes	27 (13.3)
	Simple cystic mass	16 (7.9)
	Complicated cyst	5 (2.5)
	Well-defined solid with or without coarse calcification	59 (29.1)
	Hypoechoic solid mass	77 (37.9)
	Hypoechoic solid mass with microcalcification	5 (2.5)
	Hypoechoic solid mass with microcalcification and adenopathy	4 (2.0)
Mastitis and edema	10 (4.9)	

Breast and axillary procedures were performed using a Voluson E6 (GE company, UK). A copy of the ultrasound report was obtained from medical records. Patients suspected of different types of

Table 2: The frequency of age, family history, fertility status, and location of the tumor based on benignancy and malignancy.

Variables	Benign, n (%), n = 104	Malignant, n (%), n = 99	Total N = 203	p-value
Age, years				
11–20	3 (2.9)	0 (0.0)	3 (1.5)	< 0.001
21–30	22 (21.2)	5 (5.1)	27 (13.3)	
31–40	33 (31.7)	28 (28.3)	61 (30.0)	
41–50	34 (32.7)	35 (35.4)	69 (34.0)	
51–60	8 (7.7)	16 (16.2)	24 (11.8)	
61–70	3 (2.9)	7 (7.1)	10 (4.9)	
71–80	0(0.0)	6 (6.1)	6 (3.0)	
81–90	1(1.0)	2 (2.0)	3 (1.5)	
Family history				
Yes	10 (9.6)	30 (30.3)	40 (19.7)	< 0.001
No	94 (90.4)	69 (69.7)	163 (80.3)	
Fertility status				
Fertile	87 (83.7)	54 (54.5)	141 (69.5)	< 0.001
Menopause	17 (16.3)	45 (45.5)	62 (30.5)	
Location of tumor				
Upper outer quadrant	51 (49.0)	52 (52.5)	103 (50.7)	0.690
Upper inner quadrant	12 (11.5)	11 (11.1)	23 (11.3)	
Lower outer quadrant	13 (12.5)	9 (9.1)	22 (10.8)	
Lower inner quadrant	9 (8.7)	4 (4.0)	13 (6.4)	
Central	10 (9.6)	11 (11.1)	21 (10.3)	
Multi-focal and diffuse	9 (8.7)	12 (12.1)	21 (10.3)	
Involved side				
Left	51 (49.0)	43 (43.4)	94 (46.3)	0.560
Right	41 (39.4)	40 (40.4)	81 (39.9)	
Bilateral	12 (11.5)	16 (16.2)	28 (13.8)	

malignancies (i.e., uncertain, speculation, severe hypokinesia, microcalcification, adenopathy, and complex cyst) were revisited and referred for mammography or biopsy for pathological examination or surgery (if necessary).

The necessary arrangements were made with Hamadan hospitals to provide us access to follow-up records. Patients with benign or probably benign lesions were followed-up twice at six months intervals. The subsequent ultrasound findings were compared to the initial ones in terms of tumor size and characteristics. If unchanged, the tumor was categorized as benign. The pathology reports of patients who underwent surgery were documented in their medical records. Finally, we used SPSS Statistics (SPSS Inc. Released 2007. SPSS for Windows, Version 13.0. Chicago, SPSS Inc.) to analyze the data using the *t*-test and chi-square test.

The study was approved by the Ethics Committee of Hamadan University of Medical Sciences, Hamadan, Iran. All ethical considerations, including data confidentiality, were observed. The participants could withdraw from the study at any time.

RESULTS

The demographic data and frequencies of lesion characteristics obtained from ultrasound reports are outlined in Table 1. According to our results, the mean age of the patients was 43.2 ± 12.6 years (age range: 16–87 years). The mean age of the patients with benign breast masses was 39.1 ± 11.1 years (age range: 16–83 years), and the mean age of patients with malignant breast masses was 47.5 ± 12.7 years (age range: 28–87 years). The data regarding age, family history of breast disease, fertility status, and tumor location are presented in Table 2.

Table 3: The mean of age, duration of oral contraceptive pills use, and duration of lactation of masses based on benignancy and malignancy.

Pathological type	Age, years	Duration of oral contraceptive pills use, months	Duration of lactation, months
Benign			
Fibrocystic change	42.1 ± 7.9	17.9 ± 28.4	3.8 ± 3.2
Fibroadenoma	35.1 ± 10.2	7.2 ± 14.3	2.3 ± 2.5
Abscess	32.7 ± 10.2	24.2 ± 33.7	2.1 ± 1.1
Lipoma	45.6 ± 19.5	36.6 ± 54.1	5.3 ± 3.6
Sclerosing ductal lesion	60.6 ± 16.3	15.0 ± 19.2	5.2 ± 4.5
Mammary duct ectasia	39.3 ± 3.0	30.0 ± 42.4	4.0 ± 2.0
Sclerosing adenosis	40.0 ± 11.3	20.0 ± 0.0	5.5 ± 3.5
Hydatid cyst	38.0 ± 0.0	24.9 ± 36.6	3.3 ± 0.0
Malignant			
Invasive ductal carcinoma	47.3 ± 12.3	29.4 ± 53.1	4.5 ± 3.9
Invasive papillary carcinoma	47.5 ± 12.7	-	5.9 ± 5.1
Fibrous histiocytoma	51.0 ± 0.0	60.0 ± 0.0	10.8 ± 0.0
Adenocarcinoma	61.0 ± 0.0	-	9.0 ± 3.0

We observed a significant difference between the patient’s mean age and lesion type ($p < 0.001$). The mean age, as well as the mean duration of OCP use and lactation is presented in Table 3.

The main causes of patient referral were a palpable mass, mastalgia (breast pain), mass plus mastalgia, nipple discharge, and nipple retraction in 51.2%, 17.2%, 8.4%, 4.9%, and 3.9% of patients, respectively. Additionally, the reasons for 8.9%, 3.0%, and 2.5% of the patient visits were checkup, skin problems, and edema, respectively. We found

a significant relationship between family history and malignancy ($p < 0.001$). Patients with a family history of malignant tumors were significantly more prone to malignancy ($p < 0.001$). Furthermore, there was a significant association between fertility status and tumor type ($p < 0.001$).

The mean duration of OCP use was 21.5±35.6 months. The mean duration of OCP use in patients with benign breast lesions was 17.6±30.6 months, while it was 25.6±39.9 months in those with malignant breast lesions. OCP use was not significantly related to tumor type or the pathological characteristics of the lesion ($p = 0.110$ and $p = 0.340$, respectively). The frequencies of different pathologic characteristics of masses are shown in Table 4. Furthermore, we found no significant association between the location of the tumor and its type ($p = 0.690$).

The mean duration of lactation was 4.0±3.7 months. The mean duration of lactation was 3.2±2.9 months in patients with benign breast lesions, while it was 4.8±4.2 months in those with malignant breast lesions. There was a significant difference between the two types of breast diseases in terms of duration of lactation ($p = 0.002$). We found no significant link between the involved side and the type of breast lesion ($p = 0.560$). In general, the mean mass size was 15.7±9.7 cm (13.1±8.7 cm and 9.7±18.0 cm in patients with benign and malignant breast lesions, respectively). We noted a significant association between tumor size and its type ($p = 0.001$).

Table 4: The frequency of pathologic characteristics of masses based on benignancy and malignancy.

Pathologic type	Number (%), N = 203
Benign	
Fibrocystic change	41 (20.2)
Fibroadenoma	34 (16.7)
Abscess	16 (7.9)
Lipoma	6 (3.0)
Sclerosing ductal lesion	5 (2.5)
Mammary duct ectasia	3 (1.5)
Sclerosing adenosis	2 (1.0)
Hydatid cyst	1 (0.5)
Malignant	
Invasive ductal carcinoma	71 (35.0)
Invasive papillary carcinoma	22 (10.8)
Fibrous histiocytoma	1 (0.5)
Adenocarcinoma	1 (0.5)

Ultimately, the sensitivity and specificity of ultrasound were 93.9% and 86.5%, respectively, and its positive and negative predictive values were 86.9% and 93.8%, respectively. The frequencies of false positive and true positive results were 13.1% and 86.9%, respectively, and false-negative and true negative results were observed in 6.4% and 93.8% of cases, respectively.

DISCUSSION

We observed a significant relationship between age and benign lesions, such that the majority of benign breast lesions were observed in women of childbearing age, and most of those with malignant breast masses were menopausal. In addition, there was a relationship between fertility status and breast lesion type. The frequency of breast diseases diagnosed in the progressive phases was high. Furthermore, the rate of malignancy was higher in patients with a positive family history of malignancy. In line with our findings, one study showed that breast cancer was related to family history of breast disease and the risk of malignancy increased with advancing age.⁹

It has been previously noted that the left breast was more susceptible to cancer development than the right breast¹⁰; however, our findings were not indicative of such a relationship. In the present study, the frequency of bilateral involvement was higher than in previous studies. Another study from Iran found the frequency of metastatic malignant neoplasm of the left female breast was slightly higher relative to that in the right breast¹; nonetheless, regarding the slight differences between the two studies, this result cannot be considered contradictory to our findings.

In concordance with the literature,¹⁰ we found that half of the lesions were in the upper outer quadrant. Our results marked a relationship between the location of the lesion and its type, which was confirmed previously.¹¹ The ratio of malignant to benign tumors was lower in the previously mentioned study from Iran.¹ The higher malignancy rate in our study may be due to the exclusion of medical records of patients who withdrew from treatment (probably because of benign breast disease). Additionally, in a similar study performed in the US, the ratio of benign to malignant tumors was higher compared to that reported in another study from Iran.⁷

Over and above, our study 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.¹² 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.¹² 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.¹³ The obtained sensitivity in the mentioned study was similar to the one calculated in our study; nonetheless, the specificity of ultrasound was higher in our study.

The accuracy of ultrasound has previously been estimated at 97%, while the accuracy of mammography was 87%.¹⁴ In addition, the sensitivity of ultrasound was 93% versus the 57% sensitivity of mammography. In general, the specificity and sensitivity of ultrasound were higher than those of mammography. Further, the negative predictive value of ultrasound was 99%, while it was estimated at 92% for mammography. Therefore, ultrasound is superior to mammography in the detection of invasive carcinoma when indeterminate and malignant imaging findings are taken as positive.¹⁴

The diagnostic accuracy of mammography for the detection of breast cancer was estimated higher than 87%,^{15,16} and its specificity and positive predictive value were measured to be 88% and more than 22%, respectively.¹⁶ By adopting sufficient criteria for the diagnosis of cysts, the sensitivity and specificity of ultrasound in symptomatic women were estimated at 89% and 78%, respectively.¹⁷ Our study revealed that the sensitivity and specificity of ultrasound were higher than those of mammography; however, its positive predictive value was lower.

In about 25% of the cases, solid masses are clearly distinguishable from cysts by ultrasound.¹¹ Recurrent or complex cysts can be malignant; therefore, further attention should be focused on them.¹⁸

The sensitivity and specificity of ultrasound in patients at high-risk for breast cancer were estimated at 37% and 98%, respectively.⁹ Also, its positive and negative predictive values were measured at

36% and 98.9%, respectively; the sensitivity and positive predictive value of ultrasound were higher in our study. The higher sensitivity in our study may be attributed to the fact that our patients were in advanced stages of the disease. In the majority of our patients, the reason for referral was a palpable mass in the breast. Like our study, previous studies have reported the reason for patient referral as a palpable lump in the breast in most patients.^{12,13}

It is worth mentioning that tumor volume at the time of diagnosis was larger in our study compared to other similar studies, which signifies the lack of awareness of Iranian women regarding the risk of breast cancer.^{10,19} Invasive ductal carcinoma was the most frequent malignancy in our study; however, fibrocystic changes were the most common breast diseases in other similar studies.^{10,19,20} Moreover, patients with breast cancer in our study and other similar studies in Iran were within a lower age range than those in the developed countries.²⁰ To eliminate this problem, public education programs should be held to educate women on how to identify the symptoms of breast diseases and improve the screening and diagnosis of breast cancer in Iran.

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.

The ultrasound technology for breast imaging has greatly improved in the past decade. The negative predictive value of this technique can reach 100%, whereby the required confidence for follow-up will be provided, and the need for biopsy in patients with breast lesions will be minimized.

CONCLUSION

The sensitivity and specificity of ultrasound and its positive and negative predictive values in the detection of malignant and benign lesions were high. Diagnostic ultrasound is effective for identifying benign and malignant lesions of the breast. In addition, the diagnostic accuracy of ultrasound

was high in the case of palpable masses; however, mammography is the best technique for screening and identifying patients with non-mass-like breast lesions and microcalcifications. Ultrasound is not a perfect screening technique considering the false positive and false-negative results. Future studies are recommended to study the role of ultrasound in high-risk breast cancer patients. The high rate of malignancy underscores the need for more effective public education programs, encouraging women to perform monthly breast self-examination, and training physicians and radiologists to use effective and non-invasive imaging techniques for the timely and accurate detection of lesions.

Disclosure

The authors declared no conflicts of interest. No funding was received for this study.

Acknowledgements

We extend our gratitude to the Deputy of Research and Technology and all members and experts of the Research Council of Hamadan University of Medical Sciences for their approval of the project proposal. Also, we would like to give special thanks to the Clinical Research Development Unit of Besat Hospital.

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