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Concordance and Diagnostic Accuracy of Ultrasonography and Mammography Findings with Pathology Results in Breast Cancer

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ABSTRACT

Background: Ultrasonography and mammography are two radiologic approaches for screening breast cancer; however, the pathology report is required for the ultimate diagnosis of malignancy. This study aimed to assess the concordance of ultrasonography (US) and mammography with the pathology in breast cancer.

Methods: A cross-sectional study was conducted to assess the breast US and the mammography findings based on the BI-RADS model in comparison with the definitive pathology reports in a single medical center. The sensitivity, the specificity, positive (PPV) and negative predictive value (NPV) and also the concordance between the US and the mammography data were analyzed.

Results: In this study, 126 patients were included. The sensitivity, specificity, PPV, and NPV for the US were 69.8, 71.9, 75.6 and 81.3 and for mammography were 91.9, 76.6, 80.8 and, 94.6 percent, respectively. The ROC-curve for either the US or the mammography showed that the BI-RADS 4 was accompanied with the highest sensitivity and specificity for the screening of the malignant breast lesions regarding the final diagnosis. Although an overall higher correlation between mammography report and presence of a malignant lesion was observed, the total relative concordance between the results of US and mammography as screening tools proved to be statistically significant ($P<0.01$).

Conclusion: Both the US and the mammography were sensitive and specific screening tools, particularly for the malignant breast lesions. Furthermore, when evidence of the BI-RADS≥4 in either the mammography or the US was present, utilization of the other test could be ignored before biopsy.

Introduction

The breast cancer is the first cause of cancer-related death among females between 20 and 44 years.[1,2] The incidence of new cases reached 7778 patients per year, and the specific age-related incidence reported 22.6 (95%CI 22.1-23.1) patients per every 100,000 females, with an age-standardized rate (ASR) of 27.4 (95%CI 22.5-35.9) in Iran.[2] Despite the advancement of the diagnostic and treatment tools, the median 5-years survival for the disease varies (58-85%), with regard to the fact that most survivors are treated when diagnosed in the lower stage of the disease.[1] The suspected risk factors for breast cancer include the positive family history of the disease, long term estrogen exposure, first child birth after 35 years of age, white race, Asian or Hispanic race, obesity, genetic predisposition, and the age above 50 years. The latter is the most important risk factor orchestrating the cellular breast changes towards the dysplasia and malignancy.[3,4] Currently, suspicious patients for breast cancer are screened by radiologic studies, including ultrasonography(US),

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mammography, and magnetic resonance imaging(MRI). However, the diagnosis should be confirmed by the pathology reports. The ultrasonography is a non-invasive screening procedure specifically for finding the lesions in the dense breasts. The sensitivity of the US as an operator-dependent tool is about 70-90% and specificity has been reported to be widely different.[5,6] On the other hand, the sensitivity and specificity of mammography vary between 55-90% and 70-97%, respectively.[7,8] Concurrent use of US and mammography can decrease the false-negative reports to about 0.06%[9] although in larger or more advanced tumors, the accuracy of either the US or mammography for estimating the size of the tumor has been decreased. Because of very low false-negative results of the screening studies, today, the concurrent use of the US and the mammography has been accepted as a common approach for breast tumor evaluation, preoperatively.[10] Some studies have revealed that mammography had more advantageous results than did the US for demonstrating the tumor characteristics; however, some others have contradicted this result.[2,11] Considering the review articles, the breast characteristics of every patient could be a guide to select which single available radiologic approach would be better for the patient. For example, in breasts with lower fat mass, the US and the MRI are more accurate than the mammography. This study was conducted to evaluate US and mammography findings for the breast lesions with regard to the pathologic reports.

Methods

The data was obtained from the registered medical files of the females pursuing breast examination either for the screening or diagnostic purposes (following symptoms), from May 2017 to October 2018. Ethical approval was obtained from the research ethics committee of the university (P/39/6/1/3264). The participants were randomly selected from the total of 630 registered medical files. Overall, from 252 files met inclusion criteria, and 126 samples were included through systematic random sampling. All the participants signed a written consent form for anonymous use of their data for research purposes. Exclusion criteria included the presence of inflammatory disease either locally in the breast (granulomatous mastitis) or systemic (like rheumatoid arthritis), positive history of breast, axillary or chest wall biopsy, previous thoracic surgery or irradiation, previous chemotherapy through the past 12 months of examination, presence of active skin and joint disease, ongoing pregnancy or consumption of oral contraceptives, tamoxifen or corticosteroids and need for axillary lymph node dissection. All patients were examined by a single general surgeon in a single public referral health care center. Females underwent breast examination, US and mammography study, and the breast mass biopsy was taken with core needle biopsy or open incisional or excisional approaches. The Breast Imaging-Reporting and Data System (BI-RADS) was considered for radiologic findings introduction. It is an accepted international scaling system to assess the breast mass characteristics and applied as a guide for the next step in clinical approach.7The current study considered data of the US and the mammography reports with BI-RADS 0-V. The breast US had been performed by a single radiologist. The reports of both US and mammography were interpreted for all participants by the two attending physicians of the radiology department with over 12 years of experience. Finally, all reports are reviewed and corrected according to the revisions of an experienced radiologist who was an expert in breast imaging. After every patient underwent US and mammography, she was considered a candidate for the breast mass biopsy. Based on the guidelines for the management of breast cancer, BI-RADS≥4 needs further pathology assessment while, in this study, biopsy was also taken from patients with BI-RADS 2 and 3. The reason for the latter was one of the following considerations:

1. Positive family history of breast cancer in either first or second degree relatives.
2. Positive family history of the breast cancer in a male relative.
3. Discordance between physical examination and radiologic report.
4. Patients who were considered to be unable to return for timely follow-up.
5. Patients who insisted to have a breast biopsy.

Breast biopsy was performed using one of the two following approaches by the surgeon: core needle biopsy (CNB) with the sterile 14 gauge biopsy needle (TSK ACECUT-Japan) under radiologic guide, or the surgical approach through incisional or excisional mass resection in the operating room. Specimens were sent to the reference hospital laboratory both in formalin and normal saline. The pathologic study as the definitive gold standard for making the diagnosis was performed by a single attending pathologist. The pathologic reports were classified as benign or malignant.

Demographic data in addition to US, mammography and the pathologic reports were used for analysis and interpretation. Frequency of categorical variables, central tendency statistics for continuous variables, sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predicative Value (NPV) of US and the mammography were calculated using SPSS version 21. Independent sample T test, Fisher exact test, Chi-square were used to examine the association of the variables. The Youden's index (sensitivity+specificity-1) was applied for dichotomous diagnostic tests. Statistical analysis for agreement indexes including Kendall's, Gamma and

Kappa were also run. To demonstrate the precise convergence of data, the ROC curve was customized. The significance level of *p* was considered 0.05 or the lower. Also the findings were reported in line with the STROCSS criteria.[12]

Results

The mean age (±SD) of 126 the participants was 55.2±13.9. Of all, 42(33.3%) of the study sample had positive family history of breast cancer. Considering the pathology report as the gold standard for cancer diagnosis, eventually, 76(60.3%) specimens were categorized as benign and the rest 50(39.7%) showed evidence of malignancy. Breast ultrasonography and mammography findings based on the BI-RADS are shown in Table 1.

As demonstrated in Table1, both US and mammography results demonstrated complete concordance with those of pathologic signs for th benign lesions (BI-RADS 2 and 3).The divergence between radiologic and pathologic reports was for the suspicious and/or the malignant lesions. Although mammography reports for the malignant masses (BI-RADS 5) were also fully compatible with those of the pathology, US revealed a lower diagnostic accuracy (94.3%) for distinguishing the malignant lesions($p<0.01$). The source of most disagreements between radiologic findings and those of the pathology was for the suspicious lesions (BI-RADS 4). As Table 1 shows, the concordance between pathology reports and US/mammography for malignant lesions were 94.2/71.4% respectively ($P<0.001$). Overall, the results showed that mammography reports had the highest accuracy to diagnose malignancy in BI-RADS 5 subgroup (100%) and US, with BI-RADS 4 (94.3%). Table-2 shows sensitivity, specificity, PPV, NPV and, the Youden's index for study findings.

Table 1. The concordance of US and mammography results with pathology reports

BI-RADS	Ultrasonography			Mammography			P value
	Permanent pathologic report						
	Benign	Malignant	Total	Benign	Malignant	Total	
	n (%; in row/ in column)						
0-1	0	0	0	0	0	0	N/A
2	48(100/63.2)	0	48(100/38.1)	50(100/65.8)	0	50(100/39.7)	0.7
3	25(100/32.9)	0	25(100/19.8)	22(100/28.9)	0	22(100/17.5)	0.8
4	2(5.7/2.6)	33(94.3/66.0)	35(100/27.8)	4(28.6/5.3)	10(71.4/20.0)	14(100/11.1)	<0.001
5	1(5.6/1.3)	17(94.4/34.0)	18(100/14.3)	0(0)	40(100/80.0)	40(100/31.7)	<0.01
Total	76(100/60.3)	50(100/39.7)	126(100/100)	76(100/60.3)	50(100/39.7)	126(100/100)	

Table 2 shows lower sensitivity and NPV for higher BI-RADS. This is while specificity and PPV showed an opposite pattern of association. The overall sensitivity, specificity, PPV, and NPV for US (mammography) were 69.8 (91.9), 71.9 (76.6), 75.6 (80.8), and 81.3 (94.6) percent, respectively. The Youden's index to detect breast lesions was 0.46 for US and 0.68 for mammography. Customizing ROC curve for mammography and pathology reports demonstrated that for BI-RADS 4, we had the highest overall sensitivity (94.3%) and specificity (94.5%) for screening malignancy. ROC curve for US and pathology showed the highest overall sensitivity (68-92%) and specificity (73-96%) for the BI-RADS 3 and 4. Considering the permanent pathology study for each patient, the convergence of the US and the mammography results is demonstrated in Table 3.

The colored cells in Table 3 show concordance between US and mammography results considering pathology reports as the gold standard, within each BI-RADS stratum. The overall concordance between radiology and pathology (shown as grey in Table 3) was observed in 42 subjects (33.3%).

Table 2. Diagnostic statistics for US and mammography for breast malignancy considering pathology as the gold standard findings

Radiologic modality	BI-RADS	Sensitivity	Specificity	PPV[1]	NPV[2]	Youde's index	P for Youde's index
		% (95% confident interval)					
Ultrasonography	2	96.2(94.1-97.3)	20.5(14.3-27.7)	46.7(38.3-55.4)	88.2(83.8-93.4)	0.16	
	3	92.4(89.1-95.7)	72.6(65.7-80.5)	71.0(66.6-76.4)	92.9(89.1-95.3)	0.65	
	4	67.9(59.3-73.8)	95.8(93.2-98.6)	92.3(88.2-96.4)	80.4(74.6-87.8)	0.63	
	5	22.6(11.8-34.6)	98.6(96.9-99.4)	92.3(87.4-97.3)	63.7(55.3-72.6)	0.40	
	2-5	69.8(61.6-76.3)	71.9(65.2-77.7)	75.6(70.2-80.8)	81.3(72.2-90.4)	0.46	
Mammography	2	100	32.0(20.9-45.2)	51.9(42.5-61.1)	100	0.32	<0.01
	3	98.0(96.8-99.2)	80.0(73.5-88.4)	78.8(73.4-81.9)	98.3(96.5-99.1)	0.78	
	4	94.3(92.4-96.3)	94.5(92.3-96.8)	92.5(88.6-96.4)	95.8(94.6-97.2)	0.88	
	5	75.4(68.8-80.1)	100	100	84.8(81.3-87.6)	0.75	
	2-5	91.9(87.3-95.6)	76.6(70.2-83.8)	80.8(73.8-87.5)	94.6(92.3-96.8)	0.68	

1: Positive Predictive Value 2: Negative Predictive Value

Table 3. The convergence of breast US with mammography in BI-RADS model based on pathology as the gold standard findings

		Mammography n(%)						Total n(%)
	BI-RADS	1	2	3	4	5		
US n(%)	1	6(4.8)	9(7.1)	2(1.6)	0	0	Benign	66(52.4)
	2	12(9.5)	19(15.1)	7(5.6)	1(0.8)	1(0.8)		
	3	6(4.8)	10(7.9)	1(0.8)	3(2.4)	11(8.7)		16(12.7)
	4	0	2(1.6)	0	5(4.0)	19(15.1)	Malignant	2(1.6)
	5	0	0	0	1(0.8)	11(8.7)		
		Benign			Malignant		Pathology	42(33.3%)

over-diagnosed under-diagnosed complete concordance relative concordance

Furthermore, overall complete or relative compatibility (pink and grey cells in Table3: 66+42) was observed for 108(85.7%) of cases. Furthermore, mammography over-diagnosed 12.7% of the benign lesions as malignant while the US study underestimated 1.6% of malignant lesions as the benign one.

Discussion

This study examined diagnostic accuracy and concordance of US and mammography stratified by BI-RADS and considering pathology reports as the gold standard on 126 study participants, of which 60% proved to be benign and 40% malignant. Since 1960 when mammography was first implemented, early discovery of asymptomatic breast cancer has increased and conclusively mortality rate has dropped to 25% accompanied with a 90% increase in true-positive findings.[1] Mammography is more accurate than physical examination to find masses and detect micro-calcification. Fortunately, recent results have shown that three-dimensional mammography could be even more powerful to diagnose breast malignancies and is also associated with a lower false-positive reports in comparison with the traditional type.[1] Although there are numerous studies in the medical literature on sensitivity and specificity of breast US and mammography based on definite pathology as the gold standard, the concordance between these two radiologic modalities has been less frequently investigated. This paper revealed a higher sensitivity for mammography (75.4-100%) in comparison with US (22.6-96.2%), the fact that has been confirmed by previous studies (33-56% for the US versus 36-88% for mammography).[13,14] Moreover, in each BI-RADS category, mammography was more sensitive than US. Additionally, sensitivity of both the US and mammography was lower for higher BI-RADS[13,14] while an opposite result was found for specificity which was in line with some other studies.[13,15] However, some studies have disputed this finding claiming that US was more sensitive than mammography[16-18] The differences in conclusions might be attributable to patients' characteristics in different studies (such as sample size, menopausal status of patients, genetics, and some breast characteristics, for example large breasts or breasts with higher fat composition) and/or other factors (such as instruments and equipment, and also operators' technical skills). MRI has also been introduced as a screening instrument and its concordance with US and mammography has been studied.[17-19]

The current study showed a relative concordance between US and mammography based on pathologic reports. It also revealed that findings from mammography had both a higher overall correlation with pathology and a lower underestimation of the disease in comparison to US. The US results were accompanied with over 12% overestimation of the benign lesions as malignant. However, more data needs to be carried out but this study argues that implementation of both US and mammography in breast lesions with the BI-RADS≥4 would not be necessary, when one of them is performed. Moreover, in BI-RADS 2 and 3, complete concordance with pathology was observed and no further invasive assessments were required.

This study was conducted on available patients records in a single medical center with a limited number of participants. Lack of simultaneous application of US and mammography was another limitation. Moreover, symptomatic and asymptomatic patients seeking breast screening were pooled and thus not analyzed as separate groups.

In conclusion, both ultrasonography and

mammography were shown to be sensitive and specific imaging modalities for screening breast lesions, particularly for malignancy. The relative concordance rate between these two screening modalities was acceptable. However, the overall performance of mammography was better than that of US in all breast lesions, especially for the malignant ones. US exhibited some over-diagnosis of benign lesions as malignant ones. Invasive biopsy taken in suspected cases with the BI-RADS 2 and 3 is not recommended, based on the results of the current study.

Conflicts of Interests

All authors admitted to having no financial or professional benefits to in this study.

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