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Evaluation of Clinical Assessment, Mammography, and Ultrasonography in Diagnosis of Benign and Malignant Breast Lesions and Determining Their Cost-Effectiveness

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Abstract

Background: In order to evaluate the diagnostic capabilities of various methods of breast cancer, it was expected that the use of non-invasive imaging techniques would be the earliest and the best technique of patient management.
Objectives: We attempted to evaluate mammography and ultrasonography reports along with clinical diagnosis and their agreement with the definite diagnosis of breast lesions by pathology report.
Methods: This cross sectional study was conducted on 287 women, who were referred to the cancer research center and breast clinic in Tehran between August 2016 and September 2017. The patients' basic information and their history were asked and recorded on the checklist. Also, the information obtained from the imaging report as well as the results of the pathological assessment were extracted.
Results: Compared with the pathological evaluation, the clinical assessment showed a sensitivity of 89.7%, a positive predictive value (PPV) of 97.6%, and a diagnostic accuracy of 90.24% in differentiation between malignant and non-malignant lesions. And specificity of 51.6%, and negative predictive value (NPV) of 89.2%, and a diagnostic accuracy 87.8% in differentiation between non-benign and benign lesions. Mammography had a sensitivity of 24.7%, PPV of 100%, and an accuracy of 40.2% in differentiation between malignant and non-malignant lesions. And specificity of 82.0%, NPV of 31.1%, and an accuracy of 59.0% in differentiation between non-benign and benign lesions. Ultrasonography had a sensitivity of 26%, PPV of 100%, and an accuracy of 41.44% in differentiation between malignant and non-malignant lesions. And specificity of 58.2%, NPV of 53.3%, and an accuracy of 80.6% in differentiation between non-benign and benign lesions. The cost for correct diagnosis ratio was estimated 12.31 Dollars in clinical assessment, 109.66 Dollars in mammography assessment, and 122.32 Dollars for the assessment with ultrasonography.
Conclusions: We deduced that clinical assessment was in line with pathology finding in comparison to mammography and ultrasonography in differentiation between malignant and benign lesions. In conclusion, we suggest that every radiologist pass more specialized training for reporting the mammography and ultrasonography images for declining false negative and positive results.

Keywords: Breast Cancer, Clinical Assessment, Mammography, Ultrasound

1. Background

Breast cancer is one of the most common leading causes of death in the adult female population (1, 2). The incidence of this cancer is 1 out of 8 women and the likelihood of its developing throughout the whole lifetime is 12.5% (3). The prevalence of breast cancer in Iranian women is about 120 per 100 000 persons, and the age-standardized rate is 33.21 per 100 000 persons. The peak age is reported to be in the 4th and 5th decades (4).

One of the most important factors in the patient's quality of life is the disease stage when it is diagnosed. Determining the exact size and the extension of the tumor, as well as the presence of lymphadenopathy when diagnosed, have a significant effect on the surgical type and complementary therapies. According to the review on

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breast cancer epidemiology in Iran, the 5-year survival rate was reported 67% to 73% (5); 18%, 57%, and 25% of the diagnosed patients were in stages 1, 2, and 3, respectively (5). The average 5-year survival rate of these patients was 71% (6). But, the survival rates reported by the Cancer Research Center of Shahid Beheshti University of Medical Sciences are between 5 (82%) and 10 (92%) years (7). Mammography is one of the most common non-invasive methods in breast evaluation that has high diagnostic in both screening and detection of disease. The value of mammography widely varies in different studies. Its sensitivity to the detection of cancer ranged from 55% to 90% and its specificity ranged from 70% to 97% (8, 9). Another non-invasive technique used in breast evaluation, especially in dense breasts, is ultrasonography. Ultrasound is also valuable in evaluating the uncertain findings of mammography. The results of studies have shown that the sensitivity of ultrasound in identifying the nature of breast disease is in the range of 70% to 90% (10, 11).

Since breast pathology is the standard and definitive diagnostic method and this approach is not welcomed by patients due to aggressiveness, doctors make decisions to use it, for which patients will be detected to need biopsy the masses in mammography or ultrasound.

2. Objectives

In this study, we attempted to evaluate the current status of mammography and ultrasound reports along with clinical assessment and their association with the definite diagnosis of breast lesions by pathological diagnosis. Due to the widespread use of mammography and ultrasound by the surgeons, the result of this study can be effective for non-invasively detection, diagnosis, and follow-up of the patients with breast cancer.

3. Methods

This study was carried out on women, who were referred to the cancer research center and breast clinic in Tehran between August 2016 and September 2017 with the aim of detection for breast cancer and differentiating malignant from benign lesions. The patients' basic information such as age, the history of surgery or radiotherapy, breastfeeding, job, residence area, menopausal status, menstrual age, smoking, and drug or hormone consumption was asked and recorded on the checklist by the clinician. The characteristics of suspected tumors in cancer are solid or hard consistency, non-moving, and adhesion to the surrounding tissue. Also, most of these masses are single and painless. The information obtained from the imaging (including mammography and ultrasound) as well as the results of pathological and clinical assessments were recorded on the checklist.

The study endpoint evaluated the diagnostic accuracy of clinical assessment, mammography, or ultrasound in comparison with histologic assessment (as the standard diagnosis) in assessing and distinguishing benign from malignant lesions.

The required sample size was 287 patients due to sensitivity of about 73% and specificity about 55% in Akbari et al.'s study (12).

Ethically, the patient's information was completely reserved for the researchers and no financial burden was imposed on the patients.

To assess and compare the cost-effectiveness of each assessment tool, the following equation was employed: the cost of the option divided by the effects of the procedure.

The compliance between the procedures was assessed, using the Kappa agreement analysis. Also, the sensitivity, specificity, positive and negative predictive value (NPV), and accuracy were assessed by the specific formula and using the cross-tabulation method.

The data were analyzed, using SPSS 21 (SPSS Inc., Chicago, IL) software with P values of 0.05 or less.

4. Results

In a total of 287 patients, the average age of participants was 47.70 $\pm$ 11.61 (presented as mean $\pm$ standard deviation [SD]); their age range was between 22 and 84 years and the history of smoking was found in 1.7%. Regarding job status, the majority of them (80.1%) were housewives, while 19.9% were employed. Most of the patients (95.8%) were residents in urban areas and 4.2% were in rural areas.

Breastfeeding by 2 years was 35.9% in the first pregnancy, 33.4% in the second pregnancy, and 19.9% in the third pregnancy; 28 women (9.8%) underwent previous breast surgery and 2.4% underwent the previous radiotherapy and 85 women (26.6%) were in the menopausal period and 70.4% were in the premenopausal period. The family history of breast cancer at the first and second relatives was found 9.8% and 11.5%, respectively; 64 women (22.3%) received hormone for many reasons (cosmetic and infertility). Regarding suspicious to breast lesions, 85.4% of masses were found by themselves, while other lesions were discovered during an examination by the physicians (14.6%).

To asses our clinical judgment accuracy in breast physical exam, we compared our first impression after the physical exam of 287 consecutive patients with breast masses and final pathological diagnosis; our first impression based on the physical exam only was malignant in 205,

benign in 37, and suspicious in 45 patients. Among the malignant group, 200 had malignant tumors in pathology diagnosis and 5 had benign tumors. The benign group correlated in the final pathological report in 33 cases and 4 cases had malignant tumors reported by the pathologist. The suspicious group had 26 benign and 19 malignant tumors in the final tissue diagnosis.

We compared 244 mammographic reports with the final pathologic diagnosis. Their impression based on reports only was malignant in 48, benign in 132, and suspicious in 64 patients; among the malignant group, 48 had malignant tumors in pathology diagnosis and zero had benign tumor. The benign group correlated in the final pathological reports in 41 cases and 91 cases had malignant tumors reported by the pathologist. The suspicious group had 9 benign and 55 malignant tumors in the final tissue diagnosis.

We compared 263 ultrasound reports with the final pathologic diagnosis. Their impression based on reports only was malignant in 54, benign in 60, and suspicious in 149 patients. Among the malignant group, 54 had malignant tumors in pathologic diagnosis and zero had benign tumor. The benign group correlated in the final pathologic reports in 32 cases and 28 cases had malignant tumor reports by the pathologist. The suspicious group had 23 benign and 126 malignant tumors in the final tissue diagnosis (Table 1).

Table 1. Comparison of Clinical Exam, Mammography, and Ultrasound with Pathological Finding in the Diagnosis of Benign and Malignant Breast Lesions

	Biopsy		
	Malignant, Count	Benign, Count	Total, Count
Clinical			
Malignant	200	5	205
Benign	4	33	37
Suspect	19	26	45
Total	223	64	287
Mammography			
Malignant	48	0	48
Benign	91	41	132
Suspect	55	9	64
Total	194	50	244
Ultrasound			
Malignant	54	0	54
Benign	28	32	60
Suspect	126	23	149
Total	208	55	263

Compared with the pathological evaluation, the clinical assessment showed a sensitivity of 89.7%, a positive predictive value (PPV) of 97.6%, a diagnostic accuracy of 90.24%, (Kappa = 0.744, $P < 0.001$) in differentiation between malignant and non-malignant (benign and suspected) lesions. And specificity of 51.6%, NPV of 89.2%, a diagnostic accuracy of 87.8%, (Kappa = 0.586, $P < 0.001$) in differentiation between non-benign (malignant and suspected) and benign lesions.

Mammography had a sensitivity of 24.7%, PPV of 100%, and an accuracy of 40.2%, (Kappa = 0.119, $P < 0.001$) in differentiation between malignant and non-malignant lesions. And specificity of 82.0%, NPV of 31.1%, and an accuracy of 59.0%, (Kappa = 0.218, $P < 0.001$) in differentiation between non-benign and benign lesions.

Ultrasonography had a sensitivity of 26%, PPV of 100%, and an accuracy of 41.44%, (Kappa = 0.128, $P < 0.001$) in differentiation between malignant and non-malignant lesions. And a specificity of 58.2%, NPV of 53.3%, and an accuracy of 80.6%, (Kappa = 0.433, $P < 0.001$) in differentiation between non-benign and benign lesions.

Overall, in this study, the clinical assessment was in line with the finding of pathology in comparison to mammography and ultrasonography in differentiation between malignant and benign lesions (Table 2).

According to Table 3, the Kappa coefficient of the clinical assessment for the diagnosis of malignant from benign lesions in each age group was more than mammography and ultrasonography (min Kappa = 0.485, max Kappa = 0.777).

Based on the government tariffs, the cost per clinic visits and consultation for a patient is 10 Dollars; it is 40 Dollars for mammography assessment, 40 Dollars for breast ultrasound, and about 45 Dollars for the histological assessment of breast lesions.

In this regard and according to the number of malignant and benign lesions accurately diagnosed in each assessment approaches the cost to correct diagnose ratio in:

Clinical assessment: $(10 \times 287) / (200 + 33) = 12.31$

Mammography imaging: $(40 \times 244) / (48 + 41) = 109.66$

Ultrasound imaging: $(40 \times 263) / (54 + 32) = 122.32$

The cost for correct diagnosis ratio was estimated 12.31 Dollars in clinical assessment, 109.66 Dollars in mammography assessment, and 122.32 Dollars for the assessment with ultrasonography.

We noted BI-RADS (see Appendix 1 in Supplementary File for more details) 0-1-2-3 as benign, BI-RADS 4a-b-c as suspicious, and BI-RADS 5 as malignant reports.

5. Discussion

In order to evaluate the diagnostic capabilities of various methods, including clinical evaluation and the use

Table 2. Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, and Diagnostic Accuracy in Clinical Assessment, Mammography, and Ultrasound with the Pathological Finding in Malignant from Non-Malignant (Benign and Suspected) and Non-Benign (Malignant and Suspected) form Benign Lesions

	Biopsy			SEN, 95%CI	SPE, 95%CI	PPV, 95%CI	NPV, 95%CI	Accuracy, 95%CI	Kappa, 95%CI
	Malignant, Count	Benign, Count	Total, Count						
Clinical				89.7 (84.9 - 93.3)	92.2 (82.7 - 97.4)	97.6 (94.5 - 98.9)	71.9 (63.4 - 79.2)	90.24 (86.2 - 93.4)	0.744 (P < 0.001)
Malignant	200	5	205						
Non-malignant[a]	23	59	82						
Total	223	64	287						
Mammography				24.7 (18.8 - 31.4)	100 (92.9 - 100)	100 ()	25.5 (24.0 - 27.1)	40.2 (33.9 - 46.6)	0.119 (P < 0.001)
Malignant	48	0	48						
Non-malignant	146	50	196						
Total	194	50	244						
Ultrasound				26.0 (20.1 - 32.5)	100 (93.5 - 100)	100 ()	26.3 (24.8 - 27.9)	41.44 (35.43 - 47.66)	0.128 (P < 0.001)
Malignant	54	0	54						
Non-malignant	154	55	209						
Total	208	55	263						
Clinical				98.2 (95.5 - 99.5)	51.6 (38.7 - 64.3)	87.6 (84.6 – 90.1)	89.2 (75.2 - 95.7)	87.8 (83.5 - 91.4)	0.586 (P < 0.001)
Non-benign[b]	219	31	250						
Benign	4	33	37						
Total	223	64	287						
Mammography				53.1 (45.8 - 60.3)	82.0 (68.6 - 91.4)	92.0 (86.2 – 95.5)	31.1 (27.0 - 35.5)	59.0 (52.6 - 65.3)	0.0.218 (P < 0.001)
Non-benign	103	9	112						
Benign	91	41	132						
Total	194	50	244						
Ultrasound				86.5 (81.1 - 90.9)	58.2 (44.1 - 71.4)	88.8 (85.1 – 91.5)	53.3 (43.1 - 63.3)	80.6 (75.3 - 85.2)	0.433 (P < 0.001)
Non-benign	180	23	203						
Benign	28	32	60						
Total	208	55	263						

Abbreviations: 95%CI, 95% Confidence Interval; NPV, Negative Predictive Value; PPV, Positive Predictive Value; SEN, Sensitivity; SPE, Specificity.
[a] Benign and suspected
[b] Malignant and suspected

of noninvasive methods, including mammography and ultrasound compared with the invasive biopsy method, it was expected that the use of non-invasive imaging techniques would be suitable to detect the patients who do not need pathological evaluation.

Nevertheless, our study revealed a relative low-diagnostic accuracy of each of the imaging methods in distinguishing between benign from malignant breast lesions in palpable masses. In this regard, our study showed that breast examination has an acceptable sensitivity and specificity; mammography and ultrasound also have low sensitivity and specificity in the detection of breast malignant lesions. In total, these imaging techniques only increase the likelihood of the diagnosis and prediction of malignancy and, of course, will be a good tool for screening patients. The result obtained from

Table 3. Kappa Coefficient of Clinical Assessment, Mammography, and Ultrasound for the Diagnosis of Malignant from Benign Lesions in the Age Group

Diagnoses	Age Groups, y	Agreement Coefficient	Clinical	Mammography	Ultrasound
Malignant	Low - 40	Kappa (P value)	0.726 (0.001)	0.167 (0.043)	0.128 (0.025)
		N of valid cases	74	45	73
	40 - 59	Kappa (P value)	0.738 (0.000)	0.093 (0.006)	0.107 (0.004)
		N of valid cases	167	155	151
	60 - High	Kappa (P value)	0.777 (0.000)	0.108 (0.113)	0.080 (0.202)
		N of valid cases	46	44	39
	Total	Kappa (P value)	0.744 (0.000)	0.119 (0.000)	0.128 (0.000)
		N of valid cases	287	244	263
Benign	Low - 40	Kappa (P value)	0.485 (0.000)	0.314 (0.028)	0.468 (0.000)
		N of valid cases	74	45	73
	40 - 59	Kappa (P value)	0.623 (0.000)	0.193 (0.001)	0.432 (0.000)
		N of valid cases	167	155	151
	60 - High	Kappa (P value)	0.646 (0.000)	0.214 (0.022)	-0.073 (0.624)
		N of valid cases	46	44	39
	Total	Kappa (P value)	0.586 (0.000)	0.218 (0.000)	0.433 (0.000)
		N of valid cases	287	244	263

digital mammography is more reliable in comparison with that from screen-film mammography. In our study, imaging reports were not standardized and they were problematic in demography, diagnosis, and explanation issues.

A review of another study also confirmed the results of our study by Akbari et al; 225 women were referred to the breast clinic from 2005 to 2009 with breast mass evaluated.

According to the present study, the different rates of mammography, including specificity and sensitivity were 44% and 73%, respectively. It should be noted that the false-negative rate was 17.68% (12).

Due to the importance of imaging modalities, any effort for standardizing and the improvement of their quality is prudent. What is certain is the increasing development of imaging techniques and training radiologists for the best report and clinician for the physical exam with ultrasound jointed.

Although these instances are simple, because of the importance of the best detection and do not need additional imaging and save money and time, they are our desire.

The routine positions for mammography include Mediolateral oblique (MLO) and craniocaudal (CC). Mainly, mammography is not recommended for women under 35 years provided that no specific high risk of breast cancer and abnormality in clinical examination.

On the other hand, different special photographic techniques such as spot compression magnification mammography could be more effective for the diagnosis of lesions when the conventional methods are poor to cover the whole breast problem (13).

Breast ultrasound can be used in those, who are suspected of breast lesions. It is a workable method to examine both the breast and axillary lymph nodes. The supine position is the ordinary state for applying breast ultrasound. The scan process is usually performed from the upper part of the armpits to the lower limits of breasts (including the whole breast region and armpits) (13).

Based on these results, MRI should not be used routinely for preoperative workup patients with breast cancer.

In this regard, our patients do not have any reason for doing an MRI; so, we do not have any report about MRI.

Regarding the cost-benefit calculated in our study, it also appears that there is little cost-effectiveness of the evaluation methods and, in fact, the superiority of imaging technique to clinical evaluation will still be questioned (14, 15).

5.1. Conclusions

We suggest that every radiologist willing to report mammography should be additionally trained in this special subject in order to reduce false positive and false negative reports. Besides, all breast surgeons should have been fully trained in the breast ultrasound exam; so, they can exam directly their patients and assess the accuracy of the

radiologist report and check the concordant with the physical exam. These simple educational steps can reduce the majority of mismanagement of patients due to false radiologic reports and save the patient's and clinician's time, as well. Therefore, the use of biopsy as a gold standard is considered for malignant lesions by high-level accuracy in radiologic reports.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

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Footnotes

Authors' Contribution: All authors participated in designing and writing the paper.

Conflict of Interests: All authors and co-authors have no conflict of interest.

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