

Correlation of Ultrasound & Mammography to Histopathology Results in Breast Cancer. A One Year Study at King Khalid Hospital, Najran, Saudi Arabia

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ABSTRACT

Objective: To compare the ultrasound & mammography results to histopathology reports of breast cancer cases presented in King Khalid hospital, Najran, Saudi Arabia, 2016. **Methods:** This retrospective cross-sectional analytic study was performed on 105 patients with breast lumps, who were referred to breast clinic King Khalid hospital Najran, during 2016. The patients' information was recorded using a checklist, which included name, code, age, ultrasonography, and mammography results and pathology reports. The results of ultrasonography and mammography were compared with histopathology. The results were analyzed on SPSS (version 16).

Results: The mean age of the patients was 42.3 (± 5) years. Our results showed that in histopathology reports, in (30/105) patients i.e. 28.6% were malignant, 26 patients (24.8%) biopsy revealed benign disease. Examination with mammogram revealed that, 33/105 i.e. (31.4%) were malignant and 40 cases (38.1%) had benign disease. On ultrasound examination, 21/105 (20%) were malignant and 43(40.1%) had benign disease. The mammography sensitivity was 76.6% and ultrasound sensitivity was 60%. Breast Imaging-Reporting and Data System (BIRADS) by mammogram revealed the categories as follows; category 0 in 21.9%, 2in 11.4%, 3 in 31.4, 4 in 5.7%), 4a in 6.7%, 4b in 4.8%, 4c in 1.9%, 5 in 8.6% in 6 in 4.8% and unclear in 2.9% of cases. Retro areolar area was involved in 24.8%, Upper Outer Quadrant in 45.7%, Upper Inner Quadrant in 3.8%, Lower Outer Quadrant in 4.8%, Lower Inner Quadrant in 8.6%, Diffuse involvement in 9.5% and unable to pick in 2.9%. By mammogram, the calcification found revealed 15.2% of examined patients had malignant lesions. Findings of lymph nodes examination by mammogram revealed 5.7% of the examined patients had malignant lesions. Significant difference ($P < 0.05$) regarding the age group was found in pathology and mammogram results. **Conclusion:** This study showed that mammography is the preferred diagnostic tool in screening early breast cancer patients aged above than 40 years with a higher sensitivity; the results are near to open biopsy. For the younger age group the use of ultrasonography in cases with high breast density is promising.

Keywords: Breast carcinoma, ultrasound, mammogram, comparison, histopathology.

INTRODUCTION

Breast carcinoma is the top most malignancy and is the second cause of death in the adult female's worldwide. Influencing factors for the incidence of disease include estrogen/progesterone, the age of menarche/menopause, age at first pregnancy⁽¹⁾. Out of eight, one woman is affected with a lifetime risk of about 12.5%⁽²⁾.

Breast cancer comprised 25.8% of all newly diagnosed female cancers in Saudi Arabia in 2012, thus ranking as the most common malignancy among females with tremendous socioeconomic, emotional, and public health implications⁽³⁾. The early diagnosis, by a meticulous clinical examination, staging of the disease by radiology and histopathological analysis at the time of disease presentation play an important role in deciding type of surgery and fair outcome for these patients⁽⁴⁾.

The highest incidence rate in breast cancer reported in 40- to 49-yearage group of adult women, and remaining 23% of cases of breast cancer

reported at ages lower than 40⁽⁵⁾. Considering the high incidence of advanced breast cancer at young age group (between 40–49), early diagnosis and staging the disease before surgery are important in treatment plan⁽¹⁾.

About all breast cancers are currently diagnosed by needle biopsy, there are some valid exceptions for which feasible or essential, and thus require surgical excision⁽⁶⁾. In addition, excisional biopsy of breast lump is the first biopsy choice for obvious breast cancers in certain centers, also due to cultural reasons⁽⁷⁾.

The two non-invasive radiological investigations; Ultrasonography and mammography are the important tools in early detection, prompt treatment and favorable outcome leading to increased survival rate in younger females^(8,9). Ultrasound Screening combined with mammography reduced the rate of mortality in breast cancer by 22% in women above 50years, and 15% in women aged between 49–40

years. Very important to remember, mammography sensitivity is strongly affected by breast density as one encounter denser breast in early young females, and sensitivity of mammography reduces as a result of increasing breast density by increase in age that is 30% to 48%^(8,10).

Ultrasonography and mammography are the two modalities that are available and affordable. Sensitivity of ultrasonography and mammography is different in various studies worldwide. The increasing incidence of breast cancer is a major healthcare problem, as well as its early diagnosis and treatment, can significantly affect in reducing the devastating outcome.

Although there are ample studies assessing the frequency of breast cancer in Saudi Arabia, but very lesser has compared the mammography and ultrasonography findings with pathology.

This study aimed to compare the mammography and ultrasonography findings with pathology results in patients with breast cancer, who were referred to breast clinic King Khalid hospital Najran, during 2016.

Objectives

To compare the ultrasound & mammography results to histopathology reports of breast cancer cases presented in King Khalid hospital, Najran, Saudi Arabia, 2016.

METHODOLOGY

Ethics statement

Patients with primary breast cancer who were initially diagnosed by surgical excision followed by breast-conserving surgery or mastectomy were recruited to participate in this study. Written informed consent was obtained from all the patients prior to their participation in this study. The study population came from two different sources: A proportion of the patients were diagnosed at our hospital, whereas others were referred to our hospital for definitive surgery after undergoing excision biopsy performed at an external institution. All the patients had primary breast cancer diagnosed by excision biopsy.

Study design

This is a cross sectional comparative retrospective analytic study

Study period

All the primary breast cancer cases from the surgical pathology files of the King Khalid Hospital over 1-year period (1/1/2016 up to 31/12/2016) were reviewed.

Diagnostic imaging equipment

MMG was performed using two digital full-field instruments, namely Senographe 2000D (GE Healthcare, Munich, Germany) and Selenia (Hologic GmbH, Frankfurt am Main, Germany).

Ultrasound was performed using a linear transducer with a 50-mm width and a frequency of 12 MHz, using Philips models iU22 and HD11 (Philips GmbH Healthcare, Hamburg, Germany). Real-time spatial compound imaging (CT) in combination with adaptive image processing (XRES) was a method to analyze sonographic criteria for the differentiation of benign and malignant breast lesions.

BIRADS or 'BI-RADS stands for Breast Imaging Reporting and Data System and was established by the American College of Radiology⁽¹¹⁾.

BI-RADS is a scheme for putting the findings from mammogram screening (for breast cancer diagnosis) into a small number of well-defined categories. We consider the **Categories as:** 0- incomplete, 1-negative, 2-benign findings, 3-probably benign, 4-suspicious abnormality, 5-highly suspicious of malignancy and 6-known biopsy with proven malignancy

A checklist containing patient's name, code, age, ultrasonography results (positive, suspected of negative, the presence or absence of calcification, and the number of lymph nodes), mammography results (positive, suspected of negative, the presence or absence of calcification, and the number of lymph nodes), and pathology reports (histopathological type of lesion, the presence or absence of necrosis, calcification, vascular involvement, and the number of lymph nodes) was prepared. The results of ultrasonography and mammography were compared with those of pathology, as the gold standard mean.

RESULTS

Total number of patients under studies were 105. The mean age of the patients was 42.3 (\pm 5) years. Our results showed that in histopathology reports in (30/105) patients i.e. 28.6% were malignant, 26 patients (24.8%) biopsy revealed benign disease, 44 patients (41.9%) normal report came and in 2 patients (1.9%) cellular atypia with suspicious changes were found. While examination with mammogram revealed that, 33/105 i.e. (31.4%) were malignant, 40(38.1%) had benign disease, 8(7.6%) normal and in 21(20%) suspicious changes were found and 3(2.9%) undetected. On the other hand, on ultrasound examination, 21/105 (20%) were malignant, 43(40.1%) had benign disease, 31(29.5%) normal and in 7(6.7%) suspicious

changes were found and 3(2.9%) undetected (**Table 1**).

When mammogram compared to histopathology biopsy true negative and false negative were observed in 65 (61.90%) and 7 (6.66%) patients respectively. Whereas by mammogram positive detected cases as compared to histopathology the false positive 10 (9.52%) and true positive 23 (21.9%). Moreover, the mammography sensitivity and specificity in our study was 76.6% and 86.6% respectively (**Table 2**).

When ultrasound finding as compared to histopathology biopsy true negative and false negative were observed in 72 (68.57%) and 12 (11.42%) patients respectively. Whereas by ultrasound positive detected cases as compared to histopathology the false positive 3(2.85%) and true positive 18(17.14%). The ultrasound sensitivity and specificity were 60% and 96% (**Table 3**).

Breast Imaging-Reporting and Data System (BIRADS) by mammogram revealed the categories as follows; 0(incomplete) 23(21.9%), 1(negative) 0, 2(benign findings) 12(11.4%), 3(probably benign) 33(31.4), 4(suspicious abnormality)6(5.7%), 4a(low) 7(6.7%), 4b(moderate) 5(4.8%), 4c(high) 2(1.9%), 5(highly suspicious of malignancy) 9(8.6%), 6(known biopsy with proven malignancy) 5(4.8%), unclear (Equivocal) 3(2.9%).

Other findings of mammogram was; anatomical area of breast involved, it was Retro areolar in 24.8%, Upper Outer Quadrant in 45.7%, Upper Inner Quadrant in 3.8%, Lower Outer Quadrant in 4.8%, Lower Inner Quadrant in 8.6%, Diffuse involvement of breasts in 9.5%, undetected (unable to pick) in 2.9% and no multifocal lesions was detected. By mammogram, by the found calcification we reported that, 15.2% of examined patients had malignant lesions, 8.6% benign, 67.6% had normal finding and unable to pick in 8.6% examined patients. Regarding findings of lymph nodes examination by mammogram; 5.7% malignant, 10.5% benign, 73.3% had normal findings, 4.8% suspicious of malignancy and unable to pick in 5.8% of examined patients. (**Table 1**)

By pathology results 2(11.1%) of patients with malignant aged 30-39 years while 28(32.2%) aged 40-49 years. By mammogram, the same number of patients 2(11.2%) of patients with malignant aged 30-39 years while 31(35.6%) aged 40-49 years. Also by ultrasound, the same number of patients 2(11.2%) of patients with malignant aged 30-39 years while 19(21.8%) aged 40-49 years. Significant difference ($P<0.05$) regarding the age group was found in pathology and mammogram results. (**Table 4**)

Table (1): BIRADS, Area, Mammogram results, Calcification, Ultrasound, Lymph node and Pathology findings of examined cancer breast cases, Najran, Saudi Arabia

| Age group | No. (n=105) | % | |
|-----------------------------|--|------|------|
| 30-39 | 18 | 17.1 | |
| 40-49 | 87 | 82.9 | |
| Mammogram findings | Breast Imaging-Reporting and Data System (BIRADS) | | |
| | 0(incomplete) | 23 | 21.9 |
| | 1(negative) | 0 | 0 |
| | 2(benign findings) | 12 | 11.4 |
| | 3(probably benign) | 33 | 31.4 |
| | 4(suspicious abnormality) | 6 | 5.7 |
| | 4a(low) | 7 | 6.7 |
| | 4b(moderate) | 5 | 4.8 |
| | 4c(high) | 2 | 1.9 |
| | 5(highly suspicious of malignancy) | 9 | 8.6 |
| | 6(known biopsy with proven malignancy) | 5 | 4.8 |
| | Unclear (Equivocal) | 3 | 2.9 |
| | Anatomical area of breast involved | | |
| | Retro areolar | 26 | 24.8 |
| | Upper Outer Quadrant | 48 | 45.7 |
| | Upper Inner Quadrant | 4 | 3.8 |
| | Lower Outer Quadrant | 5 | 4.8 |
| | Lower Inner Quadrant | 9 | 8.6 |
| | Diffuse involvement of breasts | 10 | 9.5 |
| | Undetected (unable to pick) | 3 | 2.9 |
| | Multifocal lesions | 0 | 0.0 |
| | Histology tumor type | | |
| | Malignant | 33 | 31.4 |
| | Benign | 40 | 38.1 |
| | Nothing (normal finding) | 8 | 7.6 |
| | Suspicious | 21 | 20.0 |
| | Undetected (unable to pick) | 3 | 2.9 |
| | Calcification | | |
| | Malignant | 16 | 15.2 |
| | Benign | 9 | 8.6 |
| | Nothing(normal finding) | 71 | 67.6 |
| | Undetected (unable to pick) | 9 | 8.6 |
| | Lymph node | | |
| Malignant | 6 | 5.7 | |
| Benign | 11 | 10.5 | |
| Nothing(normal findings) | 77 | 73.3 | |
| Suspicious | 5 | 4.8 | |
| Undetected (unable to pick) | 6 | 5.8 | |
| Ultrasound findings | Tumor type | | |
| | Malignant | 21 | 20.0 |
| | Benign | 43 | 41.0 |
| | Nothing(normal findings) | 31 | 29.5 |
| | Suspicious | 7 | 6.7 |
| | Undetected (unable to pick) | 3 | 2.9 |
| Pathology | Tumor type | | |
| | Malignant | 30 | 28.6 |
| | Benign | 26 | 24.8 |
| | Nothing(normal findings) | 44 | 41.9 |
| | Suspicious | 2 | 1.9 |

Table (2): Results of screening by mammogram versus pathology findings as a standard test

| Mammogram | Pathology | | Total |
|-----------|----------------|----------------|-------|
| | Negative | Positive | |
| Negative | 65 | 7 | 72 |
| | True negative | False negative | |
| Positive | 10 | 23 | 33 |
| | False positive | True positive | |
| Total | 75 | 30 | 105 |
| | 71.4% | 28.6% | |

From the table it is clear that;
 Sensitivity of mammogram = 76.6%
 Specificity of mammogram = 86.6%
 Positive predictive value of mammogram = 69.6%
 Negative predictive value of mammogram = 90.2%

Table (3): Results of screening by Ultrasound versus pathology findings as a standard test

| Ultrasound | Pathology | | Total |
|------------|----------------|----------------|-------|
| | Negative | Positive | |
| Negative | 72 | 12 | 84 |
| | True negative | False negative | |
| Positive | 3 | 18 | 21 |
| | False positive | True positive | |
| Total | 75 | 30 | 105 |
| | 100.0% | 100.0% | |

From the table it is clear that;
 Sensitivity of Ultrasound = 60.0%
 Specificity of Ultrasound = 96.0%
 Positive predictive value of Ultrasound = 85.7%
 Negative predictive value of Ultrasound = 85.7%

Table (4): The relationship between age group and results of Pathology, Mammogram and ultrasound in the studied cases

| | Age group (years) | | Total (n=105) | P value |
|---------------------------|-------------------|---------------|---------------|---------|
| | 30-39 (n=18) | 40- 49 (n=87) | | |
| Pathology results | | | | |
| Malignant | 2 | 28 | 30 | 0.059 |
| | 11.1% | 32.2% | 28.6% | |
| Non malignant | 16 | 59 | 75 | |
| | 88.9% | 67.8% | 71.4% | |
| Mammogram results | | | | |
| Malignant | 2 | 31 | 33 | |
| | 11.1% | 35.6% | 31.4% | |
| Non malignant | 16 | 56 | 72 | 0.033 |
| | 88.9% | 64.4% | 68.6% | |
| Ultrasound results | | | | |
| Malignant | 2 | 19 | 21 | 0.246 |
| | 11.1% | 21.8% | 20.0% | |
| Non malignant | 16 | 68 | 84 | |
| | 88.9% | 78.2% | 80.0% | |

DISCUSSION

A fewer studies has been reported in Saudi Arabia regarding comparison between the radiological investigations as ultrasound and mammogram to the tissue diagnosis (biopsy). Similar sort of our study, the age range of patients with breast cancer was between 40 and 49 years (mean: 44 years) similar to a study by **Afrah *et al.*** ⁽⁵⁾.

In our study, ductal carcinoma 41.9%, lobular cancer 28.6%, and complex cancer 24.8% were the most common types of breast cancer. Quite in line with our study, ductal carcinoma was found to be the most common type of breast cancer in other studies carried out in other countries ^(7, 9). The majority of our patients had stage 2 breast cancer. In accordance with our study, Harirchi *et al.* reported that about 96% of the patients had stage 2 breast cancer ⁽⁹⁾.

Berg *et al.* ⁽¹⁰⁾ stated that combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer, but as per literature and our study deny such correlation as mammograms carry very less radiation to be proven oncogenic ^(2,4)

Habib *et al.* ⁽¹²⁾ emphasizes that awareness and knowledge of breast cancer among Saudi Arabian ladies should be launched in some seminars describing the diagnostic modalities as ultrasound and mammogram as a part of clinical examination as a part of triple assessment for early detection of disease.

According to our study, mammography and ultrasonography results were positive in the majority of breast cancer patients, and these results were false negative in a small percentage; most of the patients are above 40 years of age. Similar to our study, the obtained results of **Farokh *et al.*** ⁽¹³⁾ showed that ultrasonography was a certain diagnostic test for detecting breast cancer in patients with high density breasts (stage 3 and 4), and mammography was more accurate than ultrasonography in determination of the size of tumor before surgery. The sensitivity and specificity of ultrasonography were compared with mammography findings and clinical examination in a study by **Shafiee *et al.*** ⁽¹⁴⁾ According to that study, the sensitivity and specificity of ultrasonography were higher than mammography examination (25.8% and 71.9% vs. 5% and 7.1%) as compared to our study in which sensitivity of mammogram = 76.6%, specificity of mammogram = 86.6% and sensitivity of ultrasound = 60.0%, specificity of ultrasound = 96.0%. Therefore, mammography was not a reliable diagnostic test in diagnosis of breast cancer ⁽¹⁴⁾. In a study by **Gharekhanloo *et al.***, the

mammography results were negative in 14.3% of patients because of high density of the breast whereas in our study it reported to be zero. For this reason, mammography is the preferred modality in screening breast cancer. Considering the incidence of breast cancer at a comparatively young age and dense breast in these ages, ultrasonography is recommended as an additional test in patients of a lower age group to increase diagnostic sensitivity as compared to mammography⁽¹⁵⁾. In our study, the sensitivity and specificity of mammography were calculated to be 73% and 55%, and the rate of false negative was 17.27%. In a study by **Haghighatkah et al.**⁽⁹⁾, the sensitivity and specificity of ultrasonography were 99% and 70%, respectively, and the rate of false negative was 17.68%. The sensitivity and specificity of color Doppler sonography and power Doppler in differentiating benign and malignant lesions were assessed in a study by Ahmadinezhad and colleagues. The results showed that the sensitivity and specificity of ultrasonography in the diagnosis of malignant tumors were 73% and 82%, respectively. In that study, sensitivity of ultrasonography was lower than that of mammography. Therefore, ultrasonography cannot be employed as a full screening test and can be applied as a complementary test to differentiate benign and malignant lesions and to avoid unnecessary biopsies⁽¹⁵⁾. The sensitivity of mammography and ultrasonography in the diagnosis of non palpable cancers was evaluated by **Leconte et al.** In our study only we have a very less patients of impalpable breast lesion i.e 9.3%. The findings indicated that the sensitivity of mammography and ultrasonography were 69% and 88% in stage 1–4, 80% and 88% in stages 1 and 2, and 56% and 88% in stages 3 and 4, respectively. In our study stage II disease was seen in 5.7% mammography is more effective in diagnosis of non-palpable cancers in stage 1–4 than ultrasonography but not in stages 1 and 2 and in dense breasts less than 30 years of age⁽¹⁶⁾. Sickles et al. study demonstrated that ultrasonography is not an acceptable substitute for mammography in diagnosis of breast cancer in few exceptional cases of lower age group and early disease⁽¹⁷⁾. A study by J. Brodersen proved that magnetic resonance imaging is more effective than ultrasonography, mammography, and clinical examination in diagnosis of residual tumors to avoid false positive results of mammogram and ultrasound. Also in patients after chemotherapy and accurate assessment of the extent of carcinoma. Long-term psychosocial consequences of false-positive screening mammography are devastating leading to anxiety, depression and ill health⁽¹⁸⁾.

Another advantage of magnetic resonance imaging is its lower costs, as compared with those for mammography and ultrasonography⁽¹⁹⁾. However, it cannot substitute mammography due to its low specificity⁽¹⁸⁾. We did not use MRI in our studies. The possible caused by biopsy and other complementary tests in women without breast cancer is one of the main concerns about screening. According to a study by **Berg et al.**, the majority of screen-detected invasive breast cancers were node-negative, and the risk of false positives decreased significantly by sonographic screening along with mammography and magnetic resonance imaging⁽¹⁰⁾. Breast cancer screening programs: in a study conducted at Saudi Arabia stated that Screening mammography is the most common and widely practiced breast cancer screening modality across the world. The major merits of breast cancer screening programs are: early diagnosis, sorting out and prevention of risk factors, and timely treatment to lessen the morbidity and reduction in 20% of mortality rate. The major demerits of breast cancer screening are over diagnosis, high cost, ionizing radiation, and their consequences. Worldwide, most countries recommend biennial screening for breast cancer at 50–74 years of age⁽²⁰⁾. However, some countries recommend screening mammography earlier, starting at the age of 40 years until 70–74 years, based on higher breast cancer incidence rate as well as in high risk patients in those countries^(20,21).

In addition, that study showed a significant difference between the sensitivity of ultrasonography in diagnosis of breast cancer and age and previous history of breastfeeding and pregnancy. This study carried out in Iran stated that mammography is the preferred modality in screening breast cancer patients; the use of complementary tests such as ultrasonography is recommended, especially in high-risk women⁽²³⁾.

CONCLUSION

This study showed that mammography is the preferred modality in screening breast cancer patients, as in our sample population used in this study was aged above than 35 years. For the younger age group use of complementary tests such as magnetic resonance imaging and ultrasonography is suggested for diagnosis of malignant and benign lesions in cases with high breast density as seen in below 30 years, increasing the speed of detection, and also reducing the costs, especially in high-risk women. Women above 40; mammogram has best results in earliest detection of disease with a higher sensitivity; the results are near to open biopsy.

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