Journal of Rawalpindi Medical College (JRMC); 2016;20(3):193-197

Original Article

Role of Ultrasound as an Adjunct Modality to Mammography in the Diagnostic Evaluation of Breast Cancer

Tehmina Sajjad Khan [1], Naushaba Malik [2], Muhammad Ishtiaq [3], Tariq Rashid [2], Shazia Fatima[4]

1.Department of Radiology, Dr. Suleman Al Habib Hospital Olaya, Riyadh-KSA;2. Department of Radiology, Punjab Employee Social Security Institute Hospital, Islamabad; 3.Shifa College of Nursing, Islamabad; 4. Department of Nuclear Medicine & Pathology, Nuclear Medicine, Oncology & Radiotherapy Institute, Islamabad

Abstract

Background: **To determine the role of ultrasound as an adjunct modality to mammography in diagnosing breast cancer.**

Methods: Total 100 patients of breast cancer were recruited in this comparative study. These cases were subjected to mammography. Ultrasound was then performed as an adjunct modality while clinical and mammographic results were available to the radiologist evaluating the ultrasound scans. Patients with positive findings were then followed for histopathology findings obtained from excisional biopsy or mastectomy specimen. The results of histopathology were taken as gold standard. Sensitivity and specificity of mammography and adjunctive ultrasound was calculated by constructing a 2 x 2 table taking histopathology as gold standard. Statistical measures of accuracy, sensitivity, specificity, positive predictive (PPV) and negative predictive values (NPV) were calculated.

Results: Age distribution revealed, 68 patients (68.0%) were ≤ 40 years of age. Mean age of the patients was 44.9 ±5.2 years. Distribution of cases by presenting symptoms was as follows: breast lump 93 (93.0%), and breast pain 7 (7.0%) with nipple discharge 10 (10.0%) and nipple retraction 8 (8.0%). Family history of breast cancer was present in 37.0%. Combined sensitivity of mammography and adjunctive ultrasound was 94.67%, specificity 77.78%, diagnostic accuracy 85.54%, positive predictive value 89.87%, negative predictive value 63.63% comparatively better than these modalities alone.

Conclusion: Ultrasound can be considered as a primary screening tool in younger population and as an adjunct to mammography in elder women to minimize the chances of missing diagnosis of breast cancers.

Key Words: Breast cancer, Mammography, Histopathology. Ultrasonography

Introduction

Breast cancer is leading cause of morbidity and mortality in females in both developed and developing world. Mammography is considered to be gold standard in screening and diagnosing breast cancer. Ultrasonography is effective in detecting lesions and distinguishing benign lesions from malignant one. Use of both tests can be more effective in diagnosing breast cancer more accurately. [1-6]

The choice of primary breast imaging in examining the women with symptoms is partly based on age. The evidences suggest that women younger than 35 years be examined with sonography and women 35 years and older be examined with mammography.[7] Ultrasound differentiates the solid masses from cysts and is more sensitive in detecting lesions in younger women with dense breast tissue. However Mammography can demonstrate non palpable breast lesion earlier than they can be diagnosed by physical examination. Mammography is less sensitive in detecting breast cancer in young patients (less than 35years) due to increased density of breast parenchyma.[8]

Mammography remains the gold standard among the imaging modalities of the breast due to its overall accuracy and relative simplicity.[9] The sensitivity and specificity of diagnostic mammography reported in various studies for diagnosing breast lesions varies from 72 to 93.2% and 84 to 87% respectively. [10,11] With about 10 million at risk women in the United States between 1 and 3 million women may get a false-negative or false-positive result.[12]

In many cases, when the diagnostic mammography shows that the abnormality is highly likely to be benign (non-cancerous) then the radiologist may

recommend follow-up mammogram, typically in six months. [13]

It is necessary to scan both whole breasts for true impression of architecture, classification of margin of lesions, distinction between benign and malignant lesions and differentiation of margin and echogenicity.[14]

With traditional ultrasonography the enhancement is no longer a distinguishing marker for a benign lesion nor is this the horizontal growing pattern but it can be good marker in computer scanning or tissue harmonic. Though colour Doppler is not routinely used in all institutions performing breast ultrasound, but colour Doppler has an additional criterion in discriminating malignant from benign lesions. It is important to observe the type of vascularisation , i.e., colour signals running straight into the lesion are a hint of malignancy, whereas angiogenesis round the border of a lesion is not. The missing of vascularization is not a proof of benignancy.[15]

3-D technique, now available in breast ultrasound by different manufacturer, is a valuable tool to obtain a detailed impression of the margins and the surroundings of a lesion in a view from so-called C-plane. In this technique star-like retraction pattern is a pathognomonic marker for malignancy, whereas a compression pattern indicates benign lesion. Carcinomas often show indeterminate surrounding in the C-plane (not definite retraction phenomenon) as well. 3-D seems to be of similar value to color Doppler in differentiating masses further, detected previously in B-Mode.[16]

Solid masses can be effectively distinguished from cysts through Ultrasonography, which account for approximately 25 percent of breast lesions.[17, 18] With strict criteria for cyst diagnosis is applied, ultrasonography has a sensitivity of 89% and a specificity of 78% in detecting abnormalities in symptomatic women.[19]Although ultrasonography is not considered a screening test but it is more sensitive in detecting lesion in women with dense breast tissues than mammography.[18, 20] It is effective in distinguishing benign solid masses from malignant diagnosing clinically palpable masses .[18,20]

Most radiologists accept breast ultrasound mainly as an adjunct to mammography: mammography always first and then after - in cases of mammographically equivocal lesions or very dense breasts – ultrasound complementary. However, that seems a traditional point of view and connected to specific interests. Under scientific and healthcare aspects the main point should be the capacity of breast ultrasound in detecting early breast carcinoma in asymptomatic women. [21].

Patients and Methods

The prospective study was undertaken in Institute of Nuclear Medicine and Oncology Lahore (INMOL) from first June 2012 to thirty first October 2013. The study participants (n=100) were female 30-60 years of age. One hundred patients referred for breast imaging were included in this study.All the patients in the study group, were imaged with mammography and bilateral whole breast ultrasound and had breast tissue biopsies. The cancer detection rate was assessed among females in between the age of 30-60 years,females having history of breast mass or breast pain, nipple discharge or retraction and any associated skin change on mammography further confirmed on ultrasound,females having positive clinical findings but missed on mammography may be due to dense breast tissue but were picked up or enhanced when ultrasound was combined. These cases were then subjected to mammography and both Cranio-caudal and Medio-lateral oblique views were obtained. A note was made of location and number oflesions. Any associated calcification, architectural distortion and asymmetric density was also noted. Ultrasound assessment was directed to the clinical or mammographic area of interest as well as whole breasts bilaterally. Patients were then followed for histopathology findings obtained from excisional biopsy or mastectomy specimen. The results of histopathology were taken as gold standard. Sensitivity and specificity of mammography and adjunctive ultrasound was calculated by constructing a 2 x 2 table taking histopathology as gold standard. Statistical measures of accuracy, sensitivity, specificity, positive predictive (PPV) and Negative predictive values (NPV) were calculated. The positive or negative cases were operationally defined. True Positive were those, which were positive for breast cancer on ultrasound, mammography and histopathology. True Negative were those which were breast cancer negative on ultrasound, mammography and histopathology. False Positive were those, which were positive for breast cancer on ultrasound and mammography but were negative on histopathology. False Negative were those, which were negative for breast cancer on ultrasound and mammography but were positive on histopathology.

Results

Mean age of the participants was 44.9 with SD $\pm$ 5.2

years. Participants had equal proportion of breast lumps on right (46) and left breast (47). Family history of breast cancer was present in 37.00% (Table 1). High frequency of masses was located in upper outer quadrant of both right (26) and left (27) breast followed by retroareolar region (14) and upper inner quadrant of right breast (13) (Table 2).

Table 1: Demographic findings and Lump location

Variable	Frequency
Age	
≥ 40 years	68
<40 years	32
Presenting symptoms	
Right Breast lump	46
Left Breast lump	47
Breast Pain	7
Family history of Breast Cancer	
Yes	37
No	63
Total	100

Table 2. Distribution of cases by mass location (Mammographic+ ultrasound findings)

Mass Location	Frequency
Right Breast	
Upper outer quadrant	26
Upper inner quadrant	13
Lower outer quadrant	1
Lower inner quadrant	5
Left Breast	
Upper outer quadrant	27
Upper inner quadrant	6
Lower outer quadrant	1
Lower inner quadrant	7
Retroareolar region	14
Total	100

On mammographic examination 74 % had masses and 52% had architectural distortion (Figure 1).On ultrasound examination 92% had solid masses and 37% had periareolar skin thickening (Figure 2). Overall sensitivity of Mammography alone was 86.05%, specificity was 63.64%, diagnostic accuracy 81.48%, positive predictive value 90.24%, negative predictive value 53.85%.Overall sensitivity of ultrasound alone was 89.87%, specificity 66.67%, diagnostic accuracy 71.50%, positive predictive value 76.34%, negative predictive value 63.64%.Overall sensitivity of mammography and adjunctive ultrasound was 94.67%, specificity 77.78%, diagnostic accuracy 85.54%, positive predictive value 89.87%, negative predictive value 63.63% (Table 3).

Table 3. Sensitivity, Specificity, Positive & Negative Predictive Value and Diagnostic Accuracy of Mammography, Ultrasound and both

Parameter	Mammography		Ultrasound		Mammography + Ultrasound	
	Estimate	95% CIs	Estimate	95% CI	Estimate	95% CI
Sensitivity	86.05%	77.18-91.83	89.87%	78.24-94.52	94.67%	87.07-97.91
Specificity	63.64%	42.95-80.27	66.67%	59.10-71.41	77.78%	67.89-81.11
Positive Predictive Value	90.24%	81.91-94.97	76.34%	66.77-83.83	89.87%	81.27-94.78
Negative Predictive Value	53.85%	35.46-71.24	63.64%	60.81-73.55	63.63%	52.45-81.34
Diagnostic Accuracy	81.48%	73.12-87.68	71%	61.46-78.99	85.54%	76.41-91.53

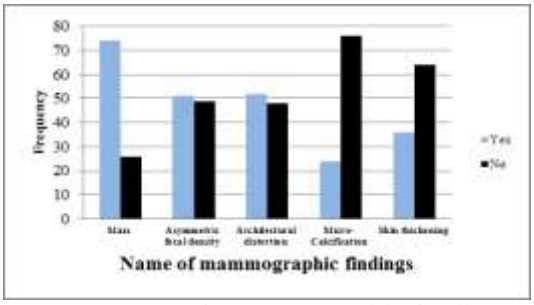

Figure 1:Frequency of mammographic findings

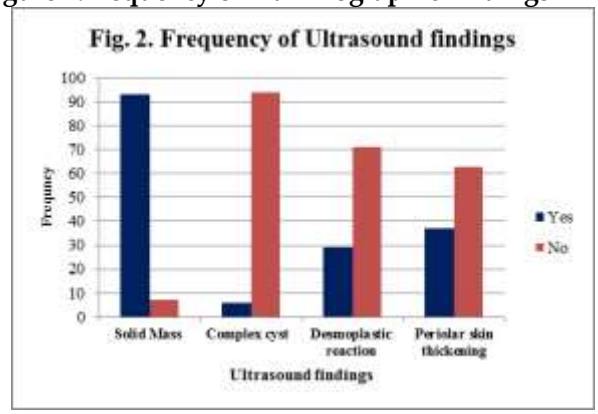

Figure 2: Frequency of ultrasound findings

Discussion

Results of present tudy indicate that the combination of ultrasound and mammography yielded enhanced sensitivity, specificity and diagnostic accuracy in the diagnostic evaluation of breast cancer. Variable and

conflicting diagnostic specificities and sensitivities of combination of both modalities mammography and adjunctive ultrasound compared with histopathology were reported in the previous literature. In present study, 93.0% of breast lumps were suspected to be breast cancer based on combined mammographic and Sonographic evaluations with 71.0% confirmed by pathologic evaluation. Reports from other studies on breast screening programs have detected very low breast cancer rates as compared to the current study.However, mammography still has some disadvantages for breast cancer detection. Although it is very sensitive, still it is not accurate in detecting breast cancer.[22] Approximately 65% of cases referred to surgical biopsy are actually benign lesions.[23]The higher breast cancer proportion in this study can be explained by the fact that it was not a screening program, and rather patients with breast lumps and breast pain along with nipple discharge and nipple retraction were referred for identification of the nature of their breast disease.

This study has 32% women of less than 40 years of age so mammographic results might not be significant in this population because mammography has limitations in detection of cancer in the dense breast tissue most commonly of young patients. The younger women tend to have dense breast tissue and numerous milk glands, making cancer detection with mammography challenging. To overcome this limitation, additional imaging modality is often needed for sound diagnosis.[24] Consequently, it has been proved earlier that sonography is more effective for women younger than 35 years of age and denser the breast parenchyma.[25-30]

Observing all these findings of previous studies regarding ultrasound as an adjunct to mammography it can be added that the overall sensitivity of the combination of mammography and ultrasonography in detecting breast cancer in the current study was about 94.67% and specificity was 77.78% which are congruent to another studies' results in which the sensitivity and specificity of combined mammography and ultrasound was 94.2% and 67.9% respectively.[31] While slightly lower that second study which indicated sensitivity and specificity of combined mammography and ultrasound as 100% and 85% respectively.[32]

Evidence suggests that in the case of a palpable lump, breast ultrasound should be the preferred imaging procedure, leading to a definitive diagnosis with an additional consecutive core needle biopsy. It should be mandatory for women without symptoms, and complementary to mammography in the case of dense breast. Adjunctive ultrasound assessment improves breast cancer detection in women of all ages and should be routinely used in symptomatic breast clinics.[33]

Conclusion

Ultrasound should be considered as an important screening and diagnostic adjunct to mammography in younger population as well as in elder women to minimize the chances of missing diagnosis of breast cancers.

References

1. Chaudhary IA, Qureshi SK, Rasul S, Bano A. Patterns of benign breast diseases. J Surg Pakistan 2003;8:5-7.
2. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, et al. Cancer statistics 2005. CA Cancer J Clin 2005;55:10-30.
3. Yip CH, Taib NA., Breast health in developing countries. Climacteric. 2014;17 Suppl 2:54-9. Retried from: http://www.ncbi.nlm.nih.gov/pubmed/25131779
4. Ryan S, McNicholas M, Eustace S, editors. Anatomy for diagnostic imaging. Spain: Saunders publishers;2004.p.307-13.
5. Houssami N, Irwig L, Simpson JM McKessar M. Sydney breast imaging accuracy study: comparative sensitivity and specificity of mammography and sonography in young women with symptoms. Am J Roentgenol 2003;180:935-40.
6. James JJ, Robin A, Wilson M, Evans AJ. Women's imaging. In: Adam A, Dixon AK, Grainger RG, Allison DJ editors. Grainger and Allison's diagnostic New York: Churchill Livingstone publishers;2008.p.1173-75.
7. Houssami N, Irwig L, Simpson JM McKessar M. Sydney breast imaging accuracy study: comparative sensitivity and specificity of mammography and sonography in young women with symptoms. Am J Roentgenol 2003;180:935-40.
8. Malik G, Waqar F, Bulede GQ. Sonomammography for evaluation of solid breast masses in young patients. J Ayub Med Coll Abbottabad 2006;18:34-37.
9. Andersson I, Sigfússon BF. Breast imaging. In: Pettersson H editor. A global textbook of radiology. Sweden: The NICER Institute publisher1995;627-68.
10. Kolata G. The New York Times: Mammograms validated as key in cancer fight [cited 2013 February 27]. Available from:
11. Poplacack SP, Tosteson AN, Grove MR, Wells WA. Mammography in 53,803 women from the New Hampshire mammography network. Radiology 2000;217:832-40.
12. Barlow WE, White E, Ballard-Barbash R, Vacek PM.Prospective breast cancer risk prediction model for women undergoing .J Natl Cancer Inst 2006;98:1204-14.
13. Kopans DB. Breast imaging and symptomatic patient: enough with the diagnostic mammography. Am J Roentgenol 2003;181:1423-24.
14. Nelson T. Early Breast Cancer Detection Using 3D Ultrasound Tomography. California Breast Cancer Research Program. cited 2012 : http://www.cbcrp.org/ .
15. Weismann C. Role of colour Doppler ultrasound in breast imaging. EJC Supplements, 2006;4:41-42.
16. Weismann C, Hergan K. Current status of 3D/ 4D volume ultrasound of the breast. Ultraschall in Med 2007;28:273-82.

17. Moss HA, Britton PD, Flower CD, Freeman AH. How reliable is modern breast imaging in differentiating benign from malignant breast lesions? Clin Radiol 1999; 54:676–82.
18. Berg WA, Campassi CI, Ioff e OB. Cystic lesions of the breast: sonographic-pathologic correlation. Radiology 2003; 227:183–91.
19. Baines CJ, Miller AB. Mammography versus clinical examination of the breasts. J Natl Cancer Inst Monogr 1997; (22):125–29.
20. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them. Radiology 2002; 225:165–75.
21. Berg WA, Blume JD, Cormack JB. Combined screening with ultrasound and mammography vs. mammography alone in women at elevated risk of breast cancer. JAMA 2008;299:2151-63.
22. Joseph YL and Carey EF. Application of artificial neural networks for diagnosis of breast cancer. In Proceedings of the Congress of Evolutionary Computation, 1999;1755-59.
23. Kopans DB. The positive predictive value of mammography. Am J Roentgenol 1992;158:521-26.
24. Breastcancer.org. Mammograms. [Online] [cited 2013 January 21]; Available from: http://www.breastcancer.org/symptoms/ .
25. Bassett LW, Ysrael M, Gold RH, Ysrael C. Usefulness of mammography and sonography in women less than 35 years of age. Radiology 1991;180:831-33.
26. Laine H, Rainio J, Arko H, Tukeva, T. Comparison of breast structure and findings by X-ray mammography, ultrasound, cytology and histology: a retrospective study. European Journal of Ultrasound 1995;2:107-11.
27. Houssami N, Ciatto S, Irwig L, Simpson JM. Comparative sensitivity of mammography and ultrasound in women with breast symptoms. Breast 2002; 11:125–30.
28. Saarenmaa I, Salminen T, Geiger U. Validity of radiological examinations of patients with breast cancer in different age groups in a population based study. Breast 2001; 1:78–81.
29. Ciatto S, Rosselli del Turco M, Catarzi S, Morrone D. The contribution of ultrasonography to the differential diagnosis of breast cancer. Neoplasma 1994; 41:341–45.
30. Mehta T. Current uses of ultrasound in the evaluation of the breast. Radiologic Clinics of North America 2003;41:841-56.
31. . Moss HA, Britton PD, Flower CD, Freeman AH. How reliable is modern breast imaging in different population, Clin Radiol. 1999, PubMed - NCBI. (n.d.).
32. Masroor I, Ahmed MN, Pasha S. To evaluate the role of sonography as an adjunct to mammography in women with dense breasts, J. Pak. Med. Assoc. 2009;59(5): 5-7
33. Hille H, Vetter M, Hackelöer BJ .Re-evaluating the role of breast ultrasound in current diagnostics of malignant breast lesions].[Article in German] 2004 ; 25(6):411-17.
34. McCavert M, O'Donnell ME, Aroori S, Badger SA. Ultrasound is a useful adjunct to mammography in the assessment of breast tumors in all patients. Int J Clin Pract. 2009;63(11):1589-94.