Diagnostic Accuracy of Ultrasonography for Evaluation Solid Breast Lesions – A Systematic Review

Syed Muhammad Yousaf Farooq¹, Guido C Robot², Syeda Khadija Tul Sughra Murrium¹, Aima Gilani¹, Hafiz Syed Arsalan Gilani¹, Syed Zain ul Abidin¹, Memona Nazir¹, Zeeshan Haider¹

¹Department of Radiology Afro Asian Institute, Lower Mall Lahore, Pakistan
²L.U Des University, Lugano, Switzerland
*youafgelani@gmail.com

Abstract:
Breast cancer in women in both developed and developing countries is the most common cancer, and remains a major public health problem.

Methods:
Analytical cross-sectional studies and only high-quality studies were included. The searched databases were: Pub Med (2008-2020), Google scholar (2008-2020) and science direct (2008-2020). The key terms searched were ultrasound imaging, Breast solid mass or lesions, papillary lesions, fibro-adenoma, breast cancer. Using these key terms, researchers found total 101 studies from the above-mentioned databases. Among these researchers found 56 studies from Google scholars, 11 from science direct and 34 from Pub Med. After this, researchers separated the relevant and irrelevant data.

Results:
Table 1 shows the Descriptive results of age from 12 studies, 17641 individuals. The mean age was 46.14697 SD 10.56736.
Table 5.2 shows the Descriptive results of sensitivity and specificity of ultrasound. The mean Sensitivity was 91.0200 and mean specificity was 89.35.
Table 3 shows the number of individuals found with benign and malignant lesions.
Table shows the pooled results of 8 studies and 2612 individuals, out of 2612 individuals we found 1220 (46.71) benign lesions and 1392 (53.29%) malignant lesions.

Conclusions:
In conclusion, Ultrasound can differentiate benign and malignant breast lesions to great extent. This technique has the potential ability to altering the handling of cases in where a biopsy may be recommended, but the risk of carcinoma is known to be relatively low. Ultrasound accuracy is recommended as the first option for follow-up examinations of lesions because of its high sensitivity and ability to detect lesions outside of breast density.

Keywords:
ultrasound, breast cancer, risk factors.

Introduction:
Breast cancer occurs from breast tissue.¹ A lump in the breast, a change of breast shape, dimpling of the skin, fluid passes from the nipple, a slightly inverted nipple, or a red or scaly patch of skin are all signs of breast cancer. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin.²

Breast cancer in women in both developed and developing countries is the most common cancer, and remains a major public health problem. It is associated with high morbidity and mortality. 1.38 million new cases and 458000 deaths occur annually worldwide.³

When compared to the Western population, Pakistani women are more likely to develop breast cancer.⁴ Breast cancer affects one out of every nine Pakistani women, making it one of Asia’s highest incidence rates.⁵

Every year, more than 1.2 million women worldwide are diagnosed with breast cancer, according to WHO statistics.⁶

In Pakistani women, breast carcinoma is the most common cancer. Breast cancer is 2.5 times more common in Pakistan than in India and Iran.
Except for Jews in Israel, Pakistan has the highest breast cancer incidence rate in Asia. Every year, at least 90,000 Pakistani women are diagnosed with breast cancer. From 1998 to 2002, the incidence of breast cancer in Karachi was 69.1 per 100,000. The fear of breast cancer is what pushes most women to seek medical help for palpable breast masses. In Africa, there are reportedly more than 600,000 people die with cancer each year. 70% of the 15 million new cancer cases per year will occur in developing countries, by 2020. Breast cancer is the most common cancer in women in South Africa. The lifetime risk of developing breast cancer is 1 in 26 women in all population groups. Breast cancer caused the deaths of over 3000 women in South Africa each year. More than 60% of women have breast cancer that has progressed locally.

Papillary breast lesions are a heterogeneous group of diseases characterized by the presence of fibro vascular cores supported by epithelial proliferation. In the duct lobular system of the breast, papillary lesions occur and usually show a cystic structure, but solid forms occur due to florid epithelial proliferation. Fibro adenomas in the teenage population are the most common strong breast masses that are excised. Fibro adenomas are classically mobile non-tender breast lesions. The diameter typically varies between 2 and 3 cm or less, although some can grow significantly bigger. The word 'giant fibro adenoma' is reserved for fibro adenomas with a diameter of 10 cm or more.

Low-level internal echoes or intra cystic debris that may layer complicated cysts. A complicated cyst does not contain dense walls, thick septa, or other solid-appearing components. The risk of malignancy is less than 2 percent among complicated breast cysts.

A well-known issue is the assessment of breast issues in young women. Most young patients have mastalgia, nodularity, or asymmetry, but a small proportion may actually have a lump. Mammography is not recommended in young people, unlike women older than 35 years, because of the low risk of breast cancer. Due to thick fibro-glandular breast tissue, the increased risk of radiation induced malignant shift and poor image quality. Ultrasoundography (USG) is the ideal form of imaging and can be useful to classify and define breast masses by certain parameters and then direct further study. Breast ultrasound is an extremely useful tool for assessment of breast lesions. Breast ultrasound may be defined as either a screening or a diagnostic test. Screening is required to detect breast abnormalities in a wide population of asymptomatic patients. The purpose of a diagnostic ultrasound is to perform a targeted evaluation to determine either a sign or a symptom, such as a palpable mass, or an abnormality is noted.

Methods:
Analytical cross-sectional studies and only high-quality studies were included.

Research Strategy:
The search was conducted in accordance with the principles of Systematic Reviews. The searched databases were: Pub Med (2008-2020), Google scholar (2008-2020) and science direct (2008-2020). The key terms searched were ultrasound imaging, solid mass or lesion, papillary lesion, fibro-adenoma, breast cancer. Using these key terms, researchers found total 30 studies from the above-mentioned data bases. Among these researchers found 10 studies from Google scholars, 2 from science direct and 18 from Pub Med. After this, researchers separated the relevant and irrelevant data, while 12 relevant and open access studies were extracted, from the searched data.

Inclusion / Exclusion Criteria and Study Design Selection
The selection criteria include those studies that include patients with breast solid mass or lesion. All irrelevant studies to our research title, randomized control/clinical trials (RCTs), and non-matched retrospective & prospective studies and chart reviews were excluded.
because of their biased results. All relevant observational (cross-sectional) studies were included.

<table>
<thead>
<tr>
<th>Author's Years</th>
<th>Study design</th>
<th>Participant of studies</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhou J et al, 2014</td>
<td>Prospective study</td>
<td>127</td>
<td>The stiffness of malignant breast lesions on the underlying tissue was greater than that of benign lesions. The strain ratio was substantially associated between the underlying tissue and the lesions and has the potential for diagnosis of breast lesions.</td>
</tr>
<tr>
<td>Fatima K et al 2018</td>
<td>Retrospective study</td>
<td>157</td>
<td>For breast lesions with possibly benign morphology, whether palpable or not, ultrasound has a 100 percent negative predictive value</td>
</tr>
<tr>
<td>Memon F et al 2017</td>
<td>Descriptive cross sectional study</td>
<td>105</td>
<td>SWE gives rise to additional useful quantitative data on solid breast lesions for gray scale ultrasound imaging. It can serve as a complementary method for breast lesion diagnosis.</td>
</tr>
<tr>
<td>Evans A et al 2012</td>
<td>Consecutive study</td>
<td>175</td>
<td>The combination of BI-RADS and grayscale ultrasound images is extremely sensitive for detecting malignancy.</td>
</tr>
<tr>
<td>Heining J et al 2008</td>
<td>Prospective study</td>
<td>2462</td>
<td>Breast ultrasound findings for malignancy has a high accuracy, equivalent to that achieved for mammography.</td>
</tr>
<tr>
<td>Chae EY et al 2016</td>
<td>Retrospective study</td>
<td>12187</td>
<td>Although the incidence of ultrasound lesions is considerably high, the rate of malignancy is very low.</td>
</tr>
<tr>
<td>Watanabe T et al 2019</td>
<td>Prospective observational study</td>
<td>1408</td>
<td>For distinguishing between benign and malignant masses, Color Doppler was found to be useful. Vascularity and the angle of incident were important and useful findings, particularly with the dominant penetrating flow pattern.</td>
</tr>
<tr>
<td>Gupta K et al 2017</td>
<td>Prospective study</td>
<td>148</td>
<td>Color Doppler and power Doppler sono-graphy are instruments that provide valuable information about the vascularity of a mass, which should also be used frequently for all breast masses to be evaluated. In the characterization of breast masses on ultrasound, Color Doppler adds important supplementary details, but in isolation, the precise distinction of benign and malignant masses is still minimal.</td>
</tr>
<tr>
<td>Bayat M et al 2017</td>
<td>Prospective study</td>
<td>108</td>
<td>With high sensitivity and specificity, ultrasound would be able to differentiate between benign and malignant breast masses.</td>
</tr>
<tr>
<td>Alawi A et al 2020</td>
<td>Retrospective study</td>
<td>203</td>
<td>There were no differences between examination using the ultrasonography and the MRI imaging compared to histo-pathological results.</td>
</tr>
<tr>
<td>Zhi H et al 2007</td>
<td>Cross-sectional study</td>
<td>296</td>
<td>Ultrasound is equivalent or better than mammography in distinguishing benign from malignant breast lesions. For examining breast lesions, ultrasound is a promising technique.</td>
</tr>
<tr>
<td>Lina J et al 2020</td>
<td>Cross-sectional study</td>
<td>78</td>
<td>To a great extent, ultrasound can distinguish between benign and malignant solid breast lesions. The number of unnecessary biopsies would be greatly decreased if these sonographic criteria is used in cases of solid breast lesions prior to biopsy for histologic analysis.</td>
</tr>
<tr>
<td>Author and Year</td>
<td>Study design</td>
<td>Sample size</td>
<td>Mean Age</td>
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<tr>
<td>14 Zhou J et al, 2014</td>
<td>Prospective study</td>
<td>199</td>
<td>48.23</td>
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<tr>
<td>Fatima K et al, 2018</td>
<td>Retrospective study</td>
<td>157</td>
<td>31.3</td>
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<td>Memon F et al, 2017</td>
<td>Descriptive cross sectional study</td>
<td>105</td>
<td>43.9</td>
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<tr>
<td>Evans A et al, 2012</td>
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<td>175</td>
<td>56</td>
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<tr>
<td>Heinig J et al, 2008</td>
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<td>2462</td>
<td>46.1</td>
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<tr>
<td>Chae EY et al, 2016</td>
<td>Retrospective study</td>
<td>12187</td>
<td>51.2</td>
</tr>
<tr>
<td>Watanabe T et al, 2019</td>
<td>Prospective observational study</td>
<td>1408</td>
<td>57.7</td>
</tr>
<tr>
<td>Gupta K et al, 2017</td>
<td>Prospective study</td>
<td>148</td>
<td>42</td>
</tr>
<tr>
<td>Bayat M et al, 2017</td>
<td>Prospective study</td>
<td>223</td>
<td>59.93</td>
</tr>
<tr>
<td>Alawi A et al, 2020</td>
<td>Retrospective study</td>
<td>203</td>
<td>24</td>
</tr>
<tr>
<td>Zhi H et al, 2007</td>
<td>Cross-sectional study</td>
<td>296</td>
<td>42</td>
</tr>
<tr>
<td>Lina J et al, 2020</td>
<td>Cross-sectional analytical</td>
<td>78</td>
<td>51.4</td>
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</table>

Results:
In flow chart of this study, our primary studies revisit 101 records. Subsequent to excluding 41 replicas, the examination of abstracts and titles identified 60 Dietary assessments of university students having substance abuse. Throughout the lists of reference of up to date articles, suitable studies and related reviews were incorporated for examination. Out of 60 reviews of studies, 30 were expelled since of not summit the addition criterion. As a result, 12 studies were suitable for final insertion in methodical review at end of selection procedure.

Table 1 shows the mean of age from 12 studies, 17641 individuals. The minimum age was 24 and maximum age was 59.93, mean age was 46.14697 so that the range was 35.93.

<table>
<thead>
<tr>
<th>Descriptive Statistics</th>
<th>N</th>
<th>Range</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>11(17641)</td>
<td>35.93</td>
<td>24.00</td>
<td>59.93</td>
<td>46.1467</td>
<td>10.56736</td>
</tr>
</tbody>
</table>

Table 2: Average Sensitivity and Specificity
Table 2 shows the pooled results of sensitivity and specificity of ultrasound which was extracted from 5 studies. The minimum sensitivity was 84.26 and maximum sensitivity was 95, mean was 91 so that the range is 10.75. Like this minimum specificity was 77 and maximum specificity was 97.50. Mean was 89.35 so that the range is 20.50.
Ultrasound has a much higher sensitivity than mammography. This may explain the different studies have reported different results, with some reporting that ultrasound has a higher specificity than mammography. Ultrasound has long been used as a reliable diagnostic method for palpable and mammographic problems. In women with dense breast tissue, ultrasonography is more sensitive than mammography in detecting lesions.

Malignancies and other masses that are not palpable masses was limited, but the only malignancy in the series was not palpable. Since palpable masses have historically been handled differently from non-palpable masses, before biopsy is deferred in this population, more studies of palpable, possibly benign masses are needed. Ultrasound had a significantly higher sensitivity and specificity for dense and heterogeneously dense breasts than mammography. Ultrasound had a sensitivity of 93.9 percent and a specificity of 86.5 percent for diagnosing malignant and benign lesions.; The positive and negative predictive values were 86.9% and 93.8 percent, respectively. Ultrasound has a 99 percent accuracy rate in the detection of malignant lesions. In a Pakistani study, The sensitivity and specificity of ultrasound for the diagnosis of breast cancer were reported to be 95.24 percent and 68.75 percent, respectively. In relation to age, the sensitivity of both tests varies. In women under the age of 45, ultrasound is more sensitive than mammography. The sensitivity was 72.6 percent, and the sensitivity of mammography was 52.1 percent. All women are at risk for developing breast cancer. The older a woman are more likely that she is to develop breast cancer. Breast cancer affects approximately 77 percent of women over the age of 50. Early detection is the most important factor in reducing breast cancer deaths. The standard imaging techniques for detecting and evaluating breast cancer is ultrasound.

<table>
<thead>
<tr>
<th>No. of studies</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>1220</td>
<td>1392</td>
</tr>
<tr>
<td>2612</td>
<td>46.71%</td>
<td>53.29%</td>
</tr>
</tbody>
</table>

Table 3: Benign and Malignant out of 8 Studies
Table 3 shows the number of individuals found with benign and malignant lesions. Table shows the pooled results of 8 studies and 2612 individuals, out of 2612 individuals we found 1220 (46.71) benign lesions and 1392 (53.29%) malignant lesions.

Discussion:
Breast solid lesions are highly common and can be detected using imaging techniques such as ultrasonography. While many of these lesions can be ignored as benign simple cysts, complex cystic and solid masses need biopsy and only symptomatic treatment. Cysts with internal debris, known as complicated cysts, are the most difficult to treat. Where the debris is mobile or a fluid-debris amount is visible, complicated cysts may be dismissed as benign. According to study, in which out of all breast masses undergoing biopsy, the malignancy rate was 55%. In terms of frequency, the majority of cancers were seen in people aged 40 to 54, The youngest patient is 28 years old, and the oldest is 79 years old. Breast cancer affects older people in developed countries.

Another research was performed about sensitivity of ultrasound for breast masses was more for benign 92% lesions. The specificity was high for malignant lesions, but the sensitivity was 67 percent. The ultrasonography sensitivity was 65 percent for breast cancer in young patients.

The implementation of sonographic criteria for benign and malignant solid masses would have helped the younger women who underwent sonography, but not mammography for the assessment of a palpable mass.

The negative sonography predictive value was 96% in non-palpable breast masses and 100% in palpable masses. In that series, the number of palpable masses was limited, but the only malignancy in the series was not palpable. Since palpable masses have historically been handled differently from non-palpable masses, before biopsy is deferred in this population, more studies of palpable, possibly benign masses are needed. Ultrasound had a significantly higher sensitivity and specificity for dense and heterogeneously dense breasts than mammography. Ultrasound had a sensitivity of 93.9 percent and a specificity of 86.5 percent for diagnosing malignant and benign lesions.; The positive and negative predictive values were 86.9% and 93.8 percent, respectively. Ultrasound has a 99 percent accuracy rate in the detection of malignant lesions. In a Pakistani study, The sensitivity and specificity of ultrasound for the diagnosis of breast cancer were reported to be 95.24 percent and 68.75 percent, respectively. In relation to age, the sensitivity of both tests varies. In women under the age of 45, ultrasound is more sensitive than mammography. The sensitivity of ultrasound was 72.6 percent, and the sensitivity of mammography was 52.1 percent. All women are at risk for developing breast cancer. The older a woman are more likely that she is to develop breast cancer. Breast cancer affects approximately 77 percent of women over the age of 50. Early detection is the most important factor in reducing breast cancer deaths. The standard imaging techniques for detecting and evaluating breast cancer is ultrasound.

Ultrasound has a much higher sensitivity than mammography. This may explain the different studies have reported different results, with some reporting that ultrasound has a higher specificity than mammography.

Ultrasound has long been used as a reliable diagnostic method for palpable and mammographic problems. In women with dense breast tissue, ultrasonography is more sensitive than mammography in detecting lesions. Malignancies and other masses that are not
detectable on mammography can be detected using ultrasound. US is increasingly used to detect early breast cancer worldwide. Ultrasound is introduced as the most effective method for diagnosing breast diseases. Ultrasonography (US) has become the first line examination for the diagnosis and characterization of breast lesions, as well as the assessment of breast cancer. In a review of the cost-effectiveness of breast cancer screening modalities, found that ultrasound screening can be cost-effective. 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.

Conclusions:
In conclusion, Ultrasound can differentiate benign and malignant breast lesions to great extent. This technique has the potential ability to altering the handling of cases in where a biopsy may be recommended, but the risk of carcinoma is known to be relatively low. Ultrasound accuracy is recommended as the first option for follow-up examinations of lesions because of its high sensitivity and ability to detect lesions outside of breast density.

References:
10- Heinig J, Witteler R, Schmitz R, Kiesel L, Steinhard J. Accuracy of classification of breast ultrasound findings based on criteria


23- Devolli-Disha E, Manxhuka-Kërliu S, Ymeri H, Kutillovci A. Comparative accuracy of mammography and ultrasound in women with breast symptoms according to age and


38- Kaplan S.S. Clinical utility of bilateral whole-breast US in the evaluation of women with dense breast tissue. Radiology. 2001


