RESEARCH ARTICLE

Diagnostic accuracy of ultrasound in the detection of malignant breast lesions

Aimuni Shafiqah Azme, Mohd Hafizi Mahmud*

Centre for Medical Imaging Studies, Faculty of Health Sciences, Universiti Teknologi MARA Cawangan Selangor Kampus Puncak Alam, 42300 Bandar Puncak Alam, Selangor, Malaysia

***Corresponding Author**

Mohd Hafizi Mahmud
Email:
mhafizi@uitm.edu.my

Abstract:

Some small lesions could be missing with mammography, particularly in dense breasts. Therefore, ultrasound is an alternative non-ionizing tool for breast imaging. This study aims to determine the diagnostic accuracy of ultrasound in detecting malignant breast lesions and the association of malignancy status with demographic and clinical factors. A total of 70 medical reports of patients who underwent breast ultrasonography between January and December 2023 were retrospectively reviewed. The lesion malignancy was validated using the biopsy as a reference standard. Diagnostic accuracy test was performed using Bayesian Theorem. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ultrasound in detecting benign and malignant breast lesions were 97.6%, 27.6%, 65.6%, and 88.9% respectively with overall diagnostic accuracy of 68.6%. The malignancy of lesions was significantly associated with age ($p = 0.015$), family history ($p = 0.004$) and fertility status ($p = 0.004$). The approximately 70% diagnostic accuracy of ultrasound suggests that this non-ionizing imaging modality could not be used independently for a definitive diagnosis of breast malignancy but needs a comprehensive integrated approach with mammography and other diagnostic imaging tools.

Keywords: Benign, breast, diagnostic accuracy, malignant, ultrasound

1. INTRODUCTION

Breast cancer is the most common cancer diagnosed in women and is usually discovered during routine screening as it evolves silently (Menon et al., 2024). It has become the leading cause of mortality and morbidity among women worldwide (Hanis et al., 2019). The major factors that can increase a woman's risk of developing breast cancer are primarily due to increased hormonal stimulation (Łukasiewicz et al., 2021). According to the Global Cancer Statistics, GLOBOCAN 2020 report, the most common cancer among Malaysian women is breast cancer followed by colorectal cancer and ovarian cancer (Tan et al., 2023).

About 99% of the cases that develop breast cancer were female (Hanis et al., 2019). People over the age of 50 years old may have a high risk of developing breast cancer (Łukasiewicz et al., 2021). BRCA1 and BRCA2 are the most vital genes responsible for an increased susceptibility to breast cancer. Both genes are commonly carried by individuals with a strong family history of breast cancer (Menon et al., 2024). Breast lesions can be classified as benign and malignant, in which benign breast lesions are non-cancerous and very common among women (Stachs et al., 2019). The most common malignant breast lesions that become major life-threatening are invasive ductal carcinoma and invasive lobular carcinoma (Menon et al., 2024).

Mammography is the first-line screening tool for breast cancer as it can detect the tumor at an early stage before clinical symptoms appear (Bhushan et al., 2021). However, some lesions cannot be detected by mammography screening alone due its lower sensitivity in the case of dense breast (Wang et al., 2022). Some breast lesions are indistinguishable in mammography due to being surrounded by fibro-glandular tissues (Gharekhanloo et al., 2018). Mammography performance can be impaired by dense breast tissue masking or obscuring noncalcified cancers because both breast cancer and dense tissue are radiopaque (Brown et al., 2023). As breast density increases, the number of false-positive results rises from 11 per 1000 exams in fatty breasts to 24 per 1000 exams in extremely dense breasts, while the sensitivity of mammography decreases from as high as 93% in fatty breasts to as low as 30% in extremely dense breasts (Kerlikowske, 2011; Weinstein et al., 2021). Therefore, ultrasound imaging is the most preferable adjunct screening tool, especially for dense breasts to detect any missing lesions on mammography and eliminate unnecessary biopsies (Ghaemian et al., 2021). However, ultrasound is a highly operator-dependent imaging modality (Sharma et al., 2021). This diagnostic technique depends mainly on the radiologist's expertise and knowledge which may result in different interpretations and diagnoses (Gharekhanloo et al., 2018). This study aims to determine the diagnostic accuracy of ultrasound in detecting malignancy of breast lesions and the association of malignancy status with demographic and clinical factors.

2. MATERIALS AND METHODS

2.1 Ethics approval

Ethics approval was granted by the Faculty Ethics Review Committee (FERC) of the Faculty of Health Sciences Universiti Teknologi MARA (FERC/FSK/MR/2024/00023) and Medical Research Ethics Committee of Ministry of Health of Malaysia (NMRR ID-24-01183-BBZ).

2.1 Ultrasound findings

This study used a retrospective cross-sectional design. The medical reports of women patients over 18 years old underwent ultrasound scanning between January to December 2023 were reviewed. The radiological findings of the ultrasound were validated against biopsy results as the reference standard. Ultrasound findings without the biopsy report were excluded from the study. The breast ultrasound was performed using a 7MHz probe (Toshiba Medical Systems Corporation). The sonographic findings were characterized based on the Breast Imaging Reporting and Data System (BIRADS) and classified into benign and malignant groups. Patients with BI-RADS assessment category ≤ 3 and assessment category ≥ 4 were classified as benign and malignant, respectively. Specifically, BI-RADS assessment categories were classified as 0 (incomplete), 1 (negative), 2 (benign), 3 (probably benign), 4A (low suspicion for malignancy), 4B (moderate suspicion for malignancy), 4C (high suspicion for malignancy), 5 (highly suggestive for malignancy) and 6 (known-biopsy proven malignancy) (American College of Radiology, 2013).

2.2 Statistical analysis

Diagnostic accuracy test (Bayesian Theorem) was performed to measure the diagnostic accuracy of ultrasound in detecting benign and malignant breast lesions. Demographic and clinical factors were presented as descriptive analysis. The Chi-Square test was conducted to determine the association of lesion malignancy with demographic and clinical factors. The statistical analyses were executed using IBM SPSS Statistics for Windows version 29.0 with $p < 0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Distribution of breast lesion malignancy

A total of 70 breast ultrasound cases were reviewed including 61 (87.1%) malignant and 9 (12.9%) benign cases. All benign cases were reported with BI-RADS score 3, while among malignant cases, 36 (59.0%), 11 (18.0%), 8 (13.1%) and 6 (9.8%) cases were reported with BI-RADS score 4a, BI-RADS score 4b, BI-RADS score 4c and BI-RADS score 5, respectively. Among these lesions, 41 (58.6%) cases were malignant, and 29 (41.4%) cases were benign. The distribution of breast lesion malignancy based on the BI-RADS assessment category is summarized in Figure 1.

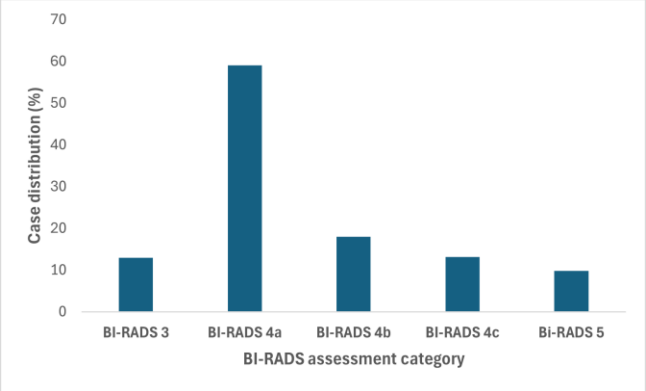

Figure 1. Distribution of breast lesion malignancy based on BI-RADS assessment category

3.2 Diagnostic accuracy of ultrasound in detecting malignancy of breast lesions

The cross-tabulation of Bayesian Theorem between ultrasound and biopsy findings are shown in Table 1.

Table 1. Cross-tabulation between ultrasound and biopsy results

Ultrasound result	**Biopsy result**		
	Malignant (positive)	Benign (negative)	Total
Malignant (positive)	40	21	61
Benign (negative)	1	8	9
Total	41	29	70

The diagnostic performance of ultrasound in detecting breast lesion malignancy is 97.6% sensitivity, 27.6% specificity, 65.6% PPV, and 88.9% NPV with an overall diagnostic accuracy of 68.6%.

The BI-RADS findings of the present study align with the expected patterns in which benign lesions are more likely to be categorized as BI-RADS 3, while higher BI-RADS scores (4a, 4b, 4c, 5) are highly suspected as malignant. BI-RADS 4 and 5 lesions generally warrant biopsy to obtain a definitive histopathological diagnosis. However, low specificity of ultrasound signifies that some benign lesions may still be incorrectly classified as BI-RADS 4 or 5, leading to unnecessary biopsies. Previous studies suggested biopsy for BI-RADS score ≤ 3 to confirm the breast lesion malignancy (Ghaemian et al., 2021; Nisar et al. 2022). BI-RADS 3 lesions are typically managed with short-term follow-up. The biopsy is considered for BI-RADS 3 lesions based on patient preference, imaging features, or accessibility of the lesion (Nisar et al., 2022). High-risk factors such as strong family history, advanced age, and palpable mass of BI-RADS 3 lesions may undergo a biopsy that may increase the false

negative results (Turk et al., 2020). The variations of reporting standards may impact the diagnostic accuracy.

In this study, ultrasound demonstrated a high sensitivity of 97.6% in detecting malignant breast lesions, indicating its effectiveness in identifying positive cases. However, the specificity was relatively low at 27.6%, suggesting that ultrasound may have a higher rate of false-positive results in identifying benign lesions. The PPV of 65.6% indicates that when ultrasound identifies a lesion as malignant, there is a 65.6% chance that the lesion is truly malignant. The NPV of 88.9% suggests that when ultrasound identifies a lesion as benign, there is an 88.9% chance that the lesions are truly benign. The high sensitivity is useful for screening out malignancy, but most of benign lesions are unnecessarily biopsied based on the ultrasound findings alone as remarked by its low specificity. The low overall diagnostic accuracy of 68.6% suggests that ultrasound is a valuable diagnostic tool for the assessment of breast lesions, but this non-ionizing modality should not be used independently for definitive diagnosis.

The current findings are consistent with the previous studies which reporting that ultrasound has a high sensitivity (> 90%) with diagnostic accuracy of 60-90% in detecting breast lesion (Siu & U.S. Preventive Services Task Force 2016; Quratulain et al., 2024). However, higher specificity (72.1% - 83.6%) was reported by those studies. The variance of diagnostic accuracy among health institutions might be contributed by multiple factors including patient population, utilization of advanced ultrasound techniques, experience of radiologist in diagnosis interpretation and reporting standard.

4.4 Association between lesion malignancy status with demographic and clinical factors

The result showed a significant association between patient's age and lesion malignancy status ($p = 0.015$). This finding is consistent with Gharekhanloo et al. (2018) and Xie et al. (2023) who note that age is a significant determinant for the development of breast cancer. Malignant breast lesions are common in older age groups, while benign lesions are common in younger age groups.

Moreover, family history was significantly associated with lesion malignancy status ($p = 0.004$). Women with inherited genetics tend to develop breast cancer compared to women with no family history. The development of proliferative lesions is associated with family history and tends to develop benign breast lesions among young women with a low tendency among advancing age (Schilling & Silva, 2020).

Furthermore, this study has demonstrated a significant association between fertility status and malignancy status ($p = 0.004$). Breast cancer tends to occur in postmenopausal women compared to young women (Hassen et al., 2022) with a 52% increased risk (Tan et al., 2018). However, no significant association was observed between the location of the lesion ($p = 0.515$) and the involved side of the lesion ($p = 0.814$) with malignancy status., which is consistent with Gharekhanloo et al. (2018). The p-values are 0.515 and 0.814 respectively. This finding suggests that the location of the lesion alone is not a reliable predictor of the nature of the lesion, and other factors such as clinical history and imaging characteristics should be considered in the diagnostic workup.

This study was limited with imbalance number of samples between benign and malignant breast lesions which might affect the low specificity value. Larger number of samples could be recommended to provide more robust and reliable estimates of the diagnostic accuracy of ultrasound in the future. Integrating ultrasound with other imaging techniques such as mammography or Magnetic Resonance Imaging (MRI), may improve the accuracy for the evaluation of breast lesions. Additionally, the application of advanced ultrasound techniques such as color Doppler and shear-wave elastography could be further explored and the consistency of ultrasound interpretation across multiple interpreters should be evaluated to identify the areas of report standardization. By addressing these future recommendations, researchers can build upon the current findings and expand their understanding of the diagnostic capabilities of ultrasound. These recommendations may facilitate more comprehensive and accurate approaches for the management of patients with suspected breast cancer.

4. CONCLUSION

Ultrasound is a valuable adjunct screening tool for breast lesions. However, the approximately 70% diagnostic accuracy of ultrasound suggests that this non-ionizing imaging modality should not be used independently for a definitive diagnosis of breast malignancy but needs a comprehensive integrated approach with mammography and other diagnostic imaging tools.

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