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Research Article

Comparative accuracy of sonography, mammography and the BI-RADS characterization of breast masses among adult women at Mulago Hospital, Uganda

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Background

Breast cancer is common among Ugandan women and mortality rate is significantly high. Uganda, like many low-income countries, has no national regular mammography screening programme, a gold standard in breast cancer imaging. Breast ultrasound and Breast Imaging Reporting and Data System (BI-RADS) classification is thus being promoted as a supplemental evaluation tool for breast masses. However, studies on the comparative accuracy of breast sonography, mammography and BI-RADS from low-income settings are limited. This study aimed to determine the accuracy of breast ultrasound, mammography and BI-RADS classification against histology in the evaluation of breast masses among adult women.

Methods

This was a cross-sectional study conducted at Mulago National Referral Hospital involving women with breast masses. The women underwent breast ultrasound, mammography and needle biopsy for histological analysis. The breast lesions were also evaluated against the BI-RADS characterization criteria.

Results

Overall, 212 breast masses were evaluated and included in the analysis. Of these, 50% (106) were benign and 50% (106) were malignant. The sensitivity for ultrasound and mammography separately was 68.5% and 72.5% respectively. The sensitivity for ultrasound and mammography combined was 85%. BI-RADS 5 category had the highest sensitivity at 59.9% while the highest specificity was noted among BI-RADS 3 and 5 at 100%. The highest accuracy was noted in the BI-RADS 5 category at 79.9%.

Conclusions

Findings from this study demonstrate that combining ultrasound and mammography could have a higher sensitivity and diagnostic accuracy than when these imaging modalities are used independently. In addition, the BI-RADS reporting classification has an optimum positive predictive value and should be promoted to standardize breast imaging reporting.

Breast cancer is the third commonest cancer in women in Uganda after Kaposi's sarcoma and cervical cancer.[1,2] The five-year survival rate is 56%.[3] Several studies have reported that breast cancer is the most common cancer and principal cause of cancer deaths in women and is, therefore, a world concern.[4-8] For example, in Brazil, breast cancer is the leading cause of cancer deaths among women.[9] Among Turkish women, breast cancer represents 24.1% of all cancers and is the second leading cause of cancer-related deaths. Earlier studies had predicted that by 2020, 70% of the 15 million new annual cancer cases will be in developing countries.[10] In South Africa breast cancer is the most common cancer in women. The lifetime risk of developing breast cancer is 1 in 26 women across all population groups. Annually, more than 3 000 women die from breast cancer in South Africa. More than 60% of women present with locally advanced breast cancer. It has been speculated that a lack of an early cancer detection programme is responsible for the majority of women presenting at a late, symptomatic stage when a cure is impossible. Umanah et al.[11] found out that other breast masses like fibroadenoma (54.8%) and fibrocystic changes (17%) were common in adolescents in a study done on an African population.

Primary randomized controlled trials have shown the importance of mammography in early diagnosis of breast cancer in asymptomatic women and it has been effective in decreasing mortality especially in women aged 50-69 years with reductions of 20% to 35%.[12] However, for the women who know about mammography, the costs involved are still very high which prevents them from going for it.[13] Besides the economic issues, other difficulties like fear of irradiation for those who know about it, limited availability of the service, anticipated pain, discomfort and anxiety about mammography also come into play.[14] It has been reported that an annual mammography for women over 50 years of age reduces mortality rate from breast cancer.[14]

Since mammography, which is the gold standard imaging modality for screening and diagnosis for women above 40 years is expensive and inaccessible to most women, especially in developing countries, the use of ultrasound and the Breast Imaging Reporting and Data System (BI-RADS) classification has been widely advocated for. The BI-RADS is an internationally recognized system of characterizing and classifying breast masses as seen at ultrasound,[15-17] and it is used by imaging professionals to structure their reporting and ease communication of imaging findings to the referring clinicians.

The Uganda Breast Cancer guidelines recognize the importance of mammography in assessing breast lesions in addition to other management procedures such as breast ultrasound, core biopsies and fine needle aspiration cytology (FNAC). Although these guidelines recognize and recommend the use of these investigative and management procedures, survival rates amongst Ugandan women are still low as compared to other parts of the world. Mammography, which is the current imaging gold standard in breast cancer screening and diagnosis for women above 40 years is not widely available and affordable to many women in Uganda. Mammography also becomes less sensitive with the more dense breasts found in
African women. In the absence of mammography, breast ultrasound has been recommended as an important evaluative tool among women with breast masses. Reasons for this are due to the easy accessibility, availability and affordability of breast ultrasound when compared to mammography. Therefore, there is a need to investigate the accuracy of breast ultrasound to inform policy and practice. From low-resource settings and especially from Sub-Saharan Africa, there has been limited literature reporting the comparative accuracy of breast ultrasound and mammography when evaluating breast masses. Women in this setting may differ in breast densities which can potentially influence the accuracy of these modalities. The purpose of this study therefore was to determine the comparative accuracy of breast ultrasound and mammography in evaluating breast masses against histology among women with breast masses from the sub-Saharan African region which would provide a comparison with what studies from other global regions have reported.

METHODS

This was a cross-sectional study involving 212 adult women with breast masses that had been referred to the radiology department for a core needle biopsy (CNB). The women were selected through consecutive sampling and they underwent breast sonography and then mammography. Based on the breast ultrasound findings, a mass was considered suspicious for malignancy if it had the following features: irregular and angular margins, posterior shadowing, had micro-lobulations, was hypoechoic, had micro-calcifications and demonstrated some flow on colour Doppler ultrasound. On mammography, the following features led to the categorization of the mass as being suspicious of malignancy: hyperdense, micro-lobulated, had microcalcifications, irregular and spiculated. BI-RADS scores for both sonography and mammography were calculated for each woman. The highest BI-RADS classification was then considered for further investigations. The BI-RADS classification was considered as follows:

- BI-RADS 3 (probably benign): ⩽ 2% malignancy risk
- BI-RADS 4A (low suspicion): >2% to ⩽10% malignancy risk
- BI-RADS 4B (moderate suspicion): >10% to ⩽50% malignancy risk
- BI-RADS 4C (high suspicion): > 50% to < 95% malignancy risk
- BI-RADS 5 (probably malignant): ⩾ 95% malignancy risk

Core needle biopsy (CNB) was performed by a radiologist using ultrasound guidance with a high frequency transducer of 8-12 MHz. 5-10 biopsies were collected and kept in formalin ready for further histological analysis in the laboratory. Surgery was based on histological reports and the decision of the surgeon. The resected masses were further analysed for pathology.

DATA ANALYSIS

The data was entered into an Epidata database and analysed using STATA 13.0 statistical package. In the BI-RADS 3 category, when a breast mass was confirmed as malignant by both imaging and histology, it was taken as a True Positive (TP) and when it was found to be benign at both imaging and histology, it was taken as True Negative (TN). False Positive (FP) was suggested when imaging pointed at malignancy, but histology did not, and False Negative (FN) was suggested when imaging suggested a benign lesion but histology reported malignancy. For BI-RADS 4A,4B,4C and 5, when both imaging and pathology suggested that a mass was malignant, this was taken as a True Positive (TP), and when it was shown to be benign by both, it was taken as True Negative (TN). False Positive (FP) was when imaging reported the mass as being malignant yet histology reported otherwise. False Negative (FN) was taken when imaging reported a benign mass yet histology reported malignancy. Sensitivity was determined as the proportion of TP: TP+FN, specificity as the proportion

Table 1. Accuracy of sonography, mammography and sonography plus mammography for malignancy

Imaging	Sensitivity (%, 95%CI)	Specificity (%, 95%CI)	PPV (%, 95%CI)	NPV (%, 95%CI)	Accuracy (%, 95%CI)
Mammography	72.5 (63.1-80.8)	43.7 (34.1-53.7)	56.1 (51-60.9)	62.1 (52.8-70.2)	49.9 (51.1-65.1)
Ultrasound	68.5 (58.8-78.1)	48.4 (38.6-58.1)	56.6 (51.4-61.8)	61 (52.5-68.7)	57.8 (51.6-64.9)
Mammography +Ultrasound	85 (76.4-91.4)	42.5 (33.2-53.1)	60.1 (55.5-64.4)	74.1 (64.1-83.2)	64.2 (57-1-70.5)

of TN: TN+FP, positive predictive value (PPV) as the proportion of TP: TP+FP, negative predictive value (NPV) as the proportion of TN: TN+FN. Accuracy was determined as the proportion of TP+TN: all women. Receiver operator characteristic (ROC) was used to determine the ability of mammography, sonography, as well as mammography and sonography, combined to predict malignancy using area under the curve (AUC).

ETHICAL CONSIDERATIONS

Approval to conduct the study was granted by the School of Health Sciences Research Ethics Committee at Makerere University (REC No: 2018-076). All these procedures of doing breast ultrasound, mammography and histo-pathology were part of the routine standard of care that is recommended for women with breast masses at Mulago Hospital. Confidentiality of the participants was ensured and informed consent was obtained to participate in the study. The study followed the Uganda Breast Cancer guidelines and each patient obtained an ultrasound report, mammography report and histology results to take to their clinicians.

RESULTS

212 women with breast masses were evaluated during the study period. Each of these had a single mass at the time of the evaluation. Therefore, 212 breast masses were evaluated. Mean age was 46.9 years. Tables 1 and 2 demonstrate the diagnostic accuracy of sonography and mammography when compared to biopsy results which was the gold standard in this study. From the CNB histology results, 106 (50%) masses were benign and 106 (50%) masses were malignant.

From table 1, the key highlight is that the sensitivity of ultrasound and mammography combined was significantly higher than the sensitivity of the individual imaging modalities when done separately. However, the specificity of ultrasound and mammography combined was somewhat reduced when compared to the separate individual specificity of either ultrasound alone or mammography alone. When ROC analysis was done in predicting breast malignancy, the combined predictive ability of mammography plus ultrasound (AUC=0.637) was higher than that of mammography alone (AUC=0.581) as well as ultrasound alone (AUC=0.585). Of the evaluated masses, 28 were BI-RADS 3; 99 masses were classified as 4A; 3 masses were classified as BI-RADS 4B; 18 were classified as BI-RADS 4C; and 64 masses as BI-RADS 5. Table 2 summarizes the sensitivity, specificity, PPV, NPV and accuracy for the individual BI-RADS classifications. The highest sensitivity was noted in BI-RADS 5 category while the highest specificity was noted among the BI-RADS 3 and 5. The highest accuracy was noted among those categorized as BI-RADS 5.

DISCUSSION

The purpose of this study was to determine the comparative accuracy of breast ultrasound and mammography in women with breast masses as well as determine accuracy of the BI-RADS characterization of breast masses among these women. Ultrasound and mammography had a comparable sensitivity in diagnosing breast malignancy. However, breast ultrasound had a higher specificity when compared to mammography. When ultrasound and mammography were combined together, the sensitivity and eventually diagnostic accuracy significantly increased compared to when each imaging modality was used independently. These findings are in resonance with some previous studies that have reported a higher combined sensitivity and accuracy of ultrasound and mammography combined when assessing breast masses for malignancy.[18-20] Therefore, it means that when evaluating breast masses to rule out malignancy, it is better to use both ultrasound and mammography as diagnostic tools rather than using only one of them. The specificity of these two combined however reduced meaning that they may not accurately rule out breast malignancy, which has also been reported previously. This reduced specificity when ultrasound was combined with mammography could be due to the fact that ultrasound can ably identify some lesions within the breast which are not yet detectable at mammography especially in women with very dense breasts. Although such studies have been reported in the more developed settings, there is a dearth of published literature reporting findings on the comparative accuracy of breast ultrasound and mammography combined from low-resource settings where breast densities of women may differ from those in high income settings. Thus findings from this study present empirical evidence from a low-resource setting.

The challenge thus posed is to decide which method is appropriate for screening. The current imaging guidelines recommend mammography screening especially for

Table 2. Accuracy of BI-RADS characterization for benign and malignant masses

BI-RADS Category	Sensitivity (%, 95%CI)	Specificity (%, 95%CI)	PPV (%, 95%CI)	NPV (%, 95%CI)	Accuracy (%, 95%CI)
3	25.6 (18.2-34.8)	100 (96.5-100)	100	57.1 (54.3-59.9)	63.1 (56-69.2)
4A	22.3 (14.9-32)	22.7 (21.1-39.2)	24.1 (17.8-32.1)	27.9 (21.9-34.6)	25.8 (21.1-33.1)
4B	2.7 (0.5-7.9)	99.3 (95.1-100)	75.2 (24-96.5)	50.5 (50.1-52.1)	51.1 (44.1-57.9)
4C	13.9 (7.9-21.8)	98.1 (92-99.3)	82.8 (60.1-94.3)	53.2 (51-54.8)	56.1 (48.7-62.5)
5	59.9 (50.3-70.1)	100 (97-100)	100	72.1 (67.1-76.1)	79.9 (74.1-84.8)

women above 40 years as the imaging gold standard. However, mammography has some limitations. For example, its sensitivity significantly reduces for women with dense breasts yet such women have an increased risk of developing breast cancer.[21,22] This is despite the fact there exists automatic systems to aid reporting such as computer aided systems that allow better performance when compared to the human reader even with dense breast during mammography.[23,24] From the findings of this study, it could be argued that adding ultrasound to the screening procedures of breast cancer is more likely to improve detection and aid early patient management. Previous literature has backed this observation.[25]

The use of breast ultrasound even gets more important in low income settings with no access to mammography equipment and with no formalised national wide mammography screening procedures for every woman to access. Part of the reasons for this relates to the huge expenses involved in setting routine mammography screening procedures. Breast ultrasound could thus be promoted as an evaluative tool as it is relatively accessible and more affordable in low income settings. The use of ultrasound as a supplemental tool to mammography in breast cancer screening continues to stimulate debate majorly because of its low PPV and likely high NPV. More studies in many different settings are thus needed to contribute to these debates.

In many settings, recommendations have been made to use the BI-RADS system to characterize breast masses as such a reporting system could be useful in discriminating benign from malignant breast masses. The accuracy rates of the BI-RADS system are still debatable ad more research in many settings is needed to contribute to evidence on how accurate BI-RADS could actually be. Findings from this study show high rates of PPV for BI-RADS 3-5. This could provide some light at the end of the tunnel as using BI-RADS can potentially discriminate between benign and malignant masses and reduce not only unnecessary biopsies, but also unnecessary surgeries, an observation that has been alluded to in previous literature.[26] The malignancy risk of BI-RADS 3 is less than 2% and most clinicians would just recommend follow up in this category of patients. Breast masses under BI-RADS 4 are not classically malignant, but are suspicious enough for core needle biopsy while BI-RADS 5 masses have higher risk of malignancy and should thus undergo biopsy.[27,28]

In imaging of suspected breast lesions, other factors come into play to affect the accuracy of imaging. For example, patient age, surgical history, characteristics of the lesion itself, menstrual and menopausal status, imaging techniques and protocols, imaging equipment used such as the use of new technologies like vacuum-assisted breast biopsy technology and many more. All these should be considered when making use of imaging accuracy results. A key limitation in this study is that breast density was not considered in the analysis and this could play a crucial role, hence taking into account of the breast density is recommended in any future studies looking at this. We also did not perform age-related sub-analysis to see how findings compare in women below 40 years and those above this age threshold, thus we recommend future studies to look into this aspect. In addition, further studies are encouraged on the accuracy of breast ultrasound and BI-RADS in other settings to further contribute to the body of evidence in considering these aspects during breast cancer screening.

CONCLUSIONS

Findings from this study demonstrate that combining ultrasound and mammography has a higher sensitivity and diagnostic accuracy of breast cancer compared to when each of these imaging modalities is used independently. In addition, the BI-RADS classification of breast masses had an optimum positive predictive value meaning that this standardized reporting on breast masses could be valuable in identifying women that urgently need biopsies and further histological analysis. The use of ultrasound should be promoted as an additional investigative layer especially in low resource settings where mammography could not easily be accessed for a significant number of women with breast masses.

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ETHICS STATEMENT

Approval to conduct the study was granted by the School of Health Sciences Research Ethics Committee at Makerere University (REC No: 2018-076). Informed consent was obtained from each participant after explaining to them the study objectives.

DATA AVAILABILITY

Data is available on reasonable request from the corresponding Author

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AUTHORSHIP CONTRIBUTIONS

AGM conceptualized the idea, wrote the proposal and draft manuscript, collected data, participated in analysis and read final manuscript; RN participated in drafting the manuscript, MG provided critical review and insight into the final manuscript.

DISCLOSURE OF INTEREST

The authors completed the ICMJE Disclosure of Interest Form (available upon request from the corresponding author) and disclose no relevant interests"

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