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Review Article

DIAGNOSTIC ACCURACY OF ABVS, CONVENTIONAL USG AND MAMMOGRAPHY AND THEIR COMPARISON IN FEMALE BREAST CANCER DETECTION WITH AND WITHOUT SYMPTOMS: A REVIEW

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ABSTRACT

Introduction and Objective: Breast cancer is frequently occurring neoplasm in female population. It is also the top five cause of death around the world in 2018. Therefore, it is a great matter of consciousness regarding female health which can be reduced by self-breast examination, clinical examination and more importantly by three imaging modalities such as MG, USG and ABVS can help in early diagnosis and treatment of breast cancer to reduce morbidity and mortality. These imaging techniques of breast are supported by histopathology report which is also called "gold standard" technique to confirm the breast pathology. In this study, the diagnostic accuracy of ABVS, conventional USG and MG with their comparison to evaluate the breast cancer detection as a diagnostic tool have been studied.

Methods: Multiple literatures search within the PubMed database, PMC database, different online medical journals through JAMA, Cochrane and Google scholar for the period 1983 to 2018; were searched to study the related articles of breast cancer detection using MG, USG and ABVS through different approach of study according to their own feasibility such as retrospective, prospective and mass campaign. Finally, these three diagnostic approaches were supported by histopathology to conform the diagnosis.

Conclusion: ABVS has a high diagnostic accuracy and better lesion size detection but the combination of ABVS and MG in dense breast is significantly better than alone which could have been sensitivity approach to 95%, may be comparable to the sensitivity of MRI.

ABVS has shown comparable diagnostic performance when combined with conventional USG but the combination of ABVS and conventional USG gives better result than single in either with symptoms or without symptoms of women.

Lesion with malignancy, USG diagnosis is more accurate than MG but the combination of both modalities diagnosed 100%. The greater accuracy of USG in diagnosis of false negative mammographic finding has proved an importance as an adjunct to MG in dense breast.

Keywords: ABVS, Breast cancer, Conventional Ultrasound, Histopathology, Mammography

INTRODUCTION

The most common presentation of the breast pathology is breast lump among females which can be benign or malignant conditions. The benign conditions like fibroadenoma, simple cyst, fibrocystic changes, duct ectasia, galactocele, and papilloma where approximately 10% of breast masses are malignant breast cancer need to be early diagnosis and treatment to reduce morbidity and mortality. The incidence of breast cancer is quite variable worldwide among females; and is also the top five cause of death around the world in 2018.[1] It is also known as a fear of cancer by psychological theory that has been known to mankind since ancient time but it was beyond medical journals and books due to fact of embarrassment.

The risk factors for breast cancer are: family history (first degree relative); delayed child bearing more than 30 years to 35years; BRCA1 and BRCA2; radiation to chest wall; increase BMI; post-menopausal estrogen/progestin hormonal therapy; early age of onset of menarche; and late age of onset of menopause.[2-5] These all are to be ruled out by taking history, clinical examination and imaging modalities such as USG, MG and ABVS. These diagnostic approaches help in early detection of breast cancers to reduce mortality and the gold standard to help is histopathology reports.

American college of radiology (ACR) of BI-RADS is used for interpretation of breast imaging modalities by radiologists around the world to reduce the variability of reports commented.[6] MG is frequently used modality of screening in early detection of breast cancer through imaging the internal structure of human breast, to show masses, calcifications and suspicious area .This mammographic screening starts at the age of 40 years annually which can decrease the chance of dying by at least 43% in recent study.[3,7] But screening with MG alone has limitation in its ability to detect tumor in the dense breast tissue. So, supplemental modality to MG, USG has been proved to depict the shape, borders and internal echo features of small in the dense breast with less than 50 years.[8] This diagnostic modality gives a significant increase cancer detection rate. Symptoms with dense breast, USG is a preferred imaging modality to evaluate the palpable breast mass, differentiation of cyst from solid nodules, evaluation of palpable lesion with associated mammographic asymmetry, and mystical cancer in mammography can be detected by ultrasonography in 10% to 40% of cases depending on the patients breast density and their age .[9-11]

ABVS is a good supplemental tool for screening breast cancer which has more reproducibility, the capacity for gathering standard views for the entire breast volume by less trained personnel, and shorter non real time review and potential for complete documentation.[12,13] It has also high reliability to detect lesion size and location in dense breast because of its additional coronal plane image which shows better observation of

lesion, margin with staging and subsequently treatment. ABVS has more accuracy than USG for breast cancer size assessment and has potential for cancer staging and surgical planning.[13,14]

MATERIAL AND METHODS

Different approaches of study were done according to their own feasibility such as retrospective, prospective, randomized control trial, cohort and mass campaign which all were approved by their own ethical board of the hospital for human investigation and informed consent of universal need for data use.

Patients:

Many literatures search were conducted within the PubMed database, PMC database, different online medical journals like JAMA and Cochrane and the Google scholar database for an additional literature search for the period 1983 to 2018. After reading these literatures, related articles were selected for the review. Approved citied studies were the search criteria and searching of explanations from cited studies were the imaging modalities of diagnosis such as conventional USG, MG, ABVS and somewhat MRI in breast pathology (symptomatic palpable masses and asymptomatic female breast) to rule out breast cancers by early detection to decrease mortality from breast cancer and is concluded as a future directions.

Conventional ultrasound examination and its imaging:

The examination is safe, convenient and reproducible where the ultrasound probe is in order of longitudinal and transverse position, from left to right, top to bottom and one by one while scanning the whole breast with axilla. Assessment of morphology, orientation, internal structures and margins of lesions through multiple planes with high resolution both in fatty breast as well as dense breast are depicted. There are characteristics shown by conventional ultrasound during imaging to differentiate between malignant and benign under the following characteristics such as shape, orientation, margin contour, echogenicity, lesions boundary, blood flow signals and posterior acoustic enhancement ; are the significant factors (table1). Ultrasound has been susceptible to the subjective factors of the examiner and is not sensitive to microcalcification. The two images are prone to overlap which affect the accuracy of diagnosis. It is also used to classify benign solid lesions with a negative predictive value (NPV) of 99.5%.[15] The measurement of tumor including the “halo” predicted tumor size for invasive lobular carcinoma with high diagnostic accuracy.[16] The Breast Imaging Reporting and Data System (BI-RADS) of American College of Radiology (The updated version, ACR 2015) has been widely used in most of the countries to reduce variability between radiologist when reporting for MG, USG, ABVS and MRI.

Lexicon	Malignant tumors	Benign tumors
Shape	Irregular	Oval, round
Orientation	Vertical, taller than wide, indifferent	Parallel, wider than tall
Margin	Indistinct	Circumscribed, identifiable, thin echogenic capsule
Margin contour	Irregular, angular, speculate	Smooth, three or fewer gentle lobulations
Echogenicity	Markedly hypo-echoic	Hyper-echoic, iso -echoic or mildly hypo-echoic
Geneity	Homogeneous	Heterogeneous
Posterior features	Shadowing	Enhancement, no changes
Calcification	Microcalcification	Absent
Surrounding tissue	Architectural distortion	Compression, no alteration
Retraction phenomena	Present	Absent

Table1: Characteristics of the Sonogram to evaluate the breast cancer

Sources: Chen et al. (2013), Gokhale at al. (2009).[17,18]

Mammography examination and imaging:

The subject is on standing position, adjusted the instrument to optimal pre-condition, and recorded the cranio-caudal view and medio-lateral oblique view of the bilateral breast with slight compression of the breast tissue. It is also widely used imaging modality to screen breast cancer. Some scholars have belief in the accuracy of MG to be 90% for calcification diagnosis. Therefore, the sensitivity and accuracy of this method for the detection early breast cancer and occult breast cancer have obvious advantages compared with other examination methods. Although MG is sensitive to calcification, it does not predominate for the internal structure of mass and relationship with surrounding tissue and there is radiation less permeable to the dense breast. So, it has significant limitations in dense glandular tissue which reduces the sensitivity in mammography and is regarded as one of the important factor that affects mammographic accuracy. Several large randomized clinical trials have also proved that MG reduced mortality in breast cancer even the recent study of MG has shown 43% of mortality reduction.[7,14]

ABVS examination and imaging:

A three dimensional (3D) ultrasound imaging technological designed specifically for breast examination .It has been configured with high resolution linear probe having maximum scanner ranges of 154mm x 168mm x 60mm and layer spacing of the acquired images is 0.5mm. The average examination time for one patient was 10 – 15 minutes. Due to characteristics of ABVS; automatic and full breast imaging with clear coronal images; ultrasound diagnosis of breast diseases has reached a new level. The system preserves complete breast information and enables multi-planar image reconstruction for retrospective analysis.[19, 20] The coronal plane is also a good indicator for the radial arrangement of mammary ducts which can display multiple

lesions on the same level and accurately locate them. It can help the surgeon to perform a record reading. Current research showed that the features in coronal images of ABVS have high value in the diagnosis of benign and malignant. ABVS is as equivalent as USG in localizing and characterizing breast cancer but more accurate to assess breast cancer size which also helps in surgical planning.[21] ABVS has also high potential in case of breast cancer staging. The benefits of ABVS have consistency and reproducibility while conventional ultrasound has operator dependency, finding depends on experience and expertise of scanning.[14,20]

Author and year	Accrual period	No. of patients	Mammography	Ultrasonography	ABVS	MG + USG	MG + ABVS
Choi WJ et al.,2014.[13]	2010-2011	5,566 women Breast cancer detection in a large population		Recall Rate(per 1000) 3.57 Cancer detection yield(per 1000) 2.7 Accuracy 96.54% SE= 62.50% SP= 96.69% PPV 7.58% NPV 99.83%	Recall Rate (per 1000) 2.57 Cancer detection yield (per 1000) 3.8 Accuracy 97.70% SE= 77.78% SP= 97.79% PPV 14.58% NPV 99.89%		
Hanan M. et al.,2018.[22]		25 patients Role of ABVS as a screening tool in detection of breast cancer	32% Negative (BIRADS) 68% (Positive) I-32%, II-28%, III-12%, IV-16%, V-12% <40 yrs =54.5% -ve = 45.5% +ve > 40 yrs = 14.3% -ve		20% Negative (BIRADS) 80% Positive (BIRADS) I-20%, II-32%, III-20%, IV-16%, V 12% SE-100%, SP-62.5% Accuracy - 88.0% PPV -85.0%		

			=85.7% +ve		NPV -100% < 40 yrs =36.4% -ve =63.6% +ve > 40 yrs =7.1% -ve = 92.9% +ve		
Hamant k. et al.,2016.[23]	2013-2015	100 patients Comparison of MG and USG with FNAC correlation	Fibroadenoma 68.18%, cystic 33% Benign cases SE- 56.75% SP – 100% PPV – 100% In case of malignant: SE – 84.61% SP – 94.58% PPV – 84.61%	Fibroadenoma 100% Cystic 100% Benign cases SE – 97.30% SP – 92.30% PPV – 97.29% In case of malignant : SE – 92.30% SP – 97.29% PPV – 92.30%		SE – 97.30% SP – 92.3% PPV – 97.29% Of total 60% benign 26% malignant 14% inflammatory Age wise 31 yrs – 40 yrs =maximum benigh > 60 yrs malignant Upper quadrant 40% In malignant case: SE – 100%	

						SP – 97.29% PPV – 92.85%	
Sachin P. et al.,2007.[24]	6month	62 patients Comparative study of MG and USG in symptomatic women (breast lump)	Fibrocystic disease - 82%, Carcinoma 77% SE – 77% total	Fibrocystic disease – 95% Carcinoma – 55% SE – 70% total		with histology report All 100% SE – 98% total	
Tiwari et al.,2017.[25]		53 patients Palpable and non-palpable breast lesions for diagnostic accuracy of MG and USG	Carcinoma – 88.88% SE – 79.24% total In case of both malignant and benign condition SE – 77.7% SP - 97.72% PPV – 87.5% NPV – 95.55%	Carcinoma 66.66% SE – 72% total In case of both malignant and benign condition SE – 55.55% SP – 97.72% PPV – 83.33% NPV – 91.48%		Carcinoma 100% SE -98% total	
Akbari ME et al.,2010.[26]	2005 - 2009	384 patients Diagnostic accuracy of MG and USG in different risk factors	< 50 yrs = SE – 69% = SP – 48% > 50 yrs = SE- 82% = SP -67% Total SE – 73% SP – 45%	< 50 yrs = SE – 68% = SP – 53% > 50 yrs = SE – 78% = SP 47% Total SE – 69% SP – 49%			

Kelly KM et al.,2010.[27]	2003 - 2007	4419 patients Diagnostic potential of MG and ABVS and combined in dense breast	SE – 14% Ductal carcinoma in situ – SE-57% Invasive carcinoma – SE -8% Invasive ductal – SE – 7% Invasive lobular – SE – 12.5% Size of invasive cancer 5mm or less – 33% 6 – 10mm – 11% 11 – 20 mm – 0% 21 – 50 mm – 17% Over 50mm – 0% Non - palpable with dense breast Fatty – SE – 0%		SE – 40% Ductal carcinoma in situ – SE-14% Invasive carcinoma – SE -44% Invasive ductal – SE – 43% Invasive lobular – SE – 50% Size of invasive cancer 5mm or less – 33% 6 – 10mm – 72% 11 – 20 mm – 30% 21 – 50 mm – 17% Over 50mm – 30% Non – palpable dense breast Fatty – SE – 50% Mixed – SE – 33%		SE – 26% Ductal carcinoma in situ – SE-28.5% Invasive carcinoma – SE -26% Invasive ductal – SE – 28.5% Invasive lobular – SE – 12.5% Size of invasive cancer 5mm or less – 33% 6 – 10mm – 17% 11 – 20 mm – 40%

			Mixed – SE – 17% Dense – SE – 17% Extra dense – 0% Dense and extra dense – SE – 14%		Dense – SE – 36% Extra dense – 71% Dense and extra dense – SE – 41%		21 – 50 mm – 17% Over 50mm –0% Non-palpable dense breast Fatty – SE – 50% Mixed – SE – 33% Dense – SE – 26% Extra dense – 14% Dense and extra dense – SE – 24%

Table 2: Diagnostic approach and performance of three modality of imaging in breast cancer (sensitivity and specificity)

DISCUSSION

Breast lesion is the major health problems in women specially breast cancer that remains one of the vital causes of death in women over the age of 40 years.[28] So, it is the great matter of consciousness in female health to be aware of being suffered from some kind of breast pathologies which need to be reduced by early diagnosis and treatment with the help of self-breast examination, clinical examination and imaging modalities such as MG, USG and ABVS. These imaging modalities are finally supported by histopathology report which is the gold standard technique to conform the breast pathology.

Considering the low record rate 2.57 per 1000 and the PPV of 14.58% in ABVS compared with conventional ultrasound, ABVS is a very nice supplemental tool in breast cancer screening (Woo Jung Choi et al. 2014).[13] There was also cancer detection rate of 3.8 per 1000 in ABVS subject, which is higher than both a previous studies showed 2.6 per 1000 for cancer detection rate with ABVS and the supplemental yield of earlier study using conventional ultrasound (range, 2.7- 4.6 per 1000) (Berg, 2009).[12] The accuracy ,sensitivity and specificity of ABVS were found to be 97.70%, 77.78%, and 97.79% respectively(Woo Jung Choi et al.2014).[13] These are significantly higher than Ultrasound but the absolute value was little different. This result was similar to previous study (Kotsianus-Hermle et al., 2009; wang et al., 2012).[29,30]

The size of a breast cancer lesion plays an important role in staging and subsequent treatment. The mean size of the breast tumor was 17.9mm in ABVS group and 13.8mm in conventional ultrasound group respectively. If defined to invasive cancer, the mean size of the tumors are 12.4mm in ABVS group and 12.7mm in conventional ultrasound group which indicates the benefit of detecting smaller lesion (Woo Jung Choi et al. 2014).[13]

We know that MG is studied the best in breast screening modality for women of general population. A mammographic breast density is a strong predictor of breast cancer risk.[31]

The aim to automate breast ultrasound are: Decreasing radiologist's time per case. Produce a standardized high quality examination that improves the conspicuity of cancers (Hanan M. et al., 2018).[22] The reproducibility of ABVS can eliminate the investigation-dependent and non-standardized documentation.[32] These characteristics make ABVS a very meaningful additional diagnostic breast screening. The ABVS has high diagnostic accuracy, better lesion size prediction, operator- independent, visualization of whole breast and can do examination in women with mammographic contraindication (Hanan M. et al. 2018).[22]

Out of 44 cases of fibroadenoma MG detected 68.18% cases while USG detected 100% cases and combined diagnosed 100% cases. So, USG is the investigation of choice for young female with palpable breast mass (Kumar H et al., 2016).[23] These results are comparable to study done by Ghazala Malik et al 2006.[33] In case of cystic disease MG diagnosed only 33% whereas USG diagnosed 100% which is an indication of USG to differentiate solid from cystic lesions (Kumar H et al. 2016).[23] The sensitivity, specificity and PPV of MG in case of benign lesions were 56.75%, 100% and 100% where sensitivity of USG was 97.30%, specificity was 92.3% and PPV was 92.29%.

MG detected 84.61% of malignant cases while USG diagnosed 92.30% cases and combination of both modalities diagnosed 100%. So, combination of both modalities detected approximately 15% and 8% more palpable malignancies than MG and USG alone respectively (Kumar H et al. 2016).[23]

Small wood JA et al.[34] found USG to be both more sensitive (93%) and specificity (95%) in a large retrospective series of 1000 patients undergoing investigation for symptomatic breast disease. Consequently series of 142 patients undergoing surgery where histological conformation was done; USG was more sensitive (91%) and specificity (81%) (Kumar H et al. 2016).[23] In both studies, the greater accuracy of USG showed its ability to diagnose lesions hidden in x-ray dense breast and where MG has revealed features unknown nature asymmetrical densities. In these instances USG proved its importance as an adjunct to MG in the preoperative assessment of breast lesion.[35]

S.R.C Benson et al.[36] concluded USG is better than MG for detecting invasive breast cancer. The combined USG and MG is better than either modality used alone, a 9% increase in breast cancer was found by combined approach.

Vessel density in fibroadenoma is more uniform throughout the tumor than it is in carcinoma, with no statistically significant difference between periphery and center. This can be identified by using color Doppler USG where positive rim sign or rim enhancing carcinomas were observed to have varying degrees of central desmoplasia, associated with lower vessel density. Rim enhancing was observed in 5 of 16 carcinomas, but none of the rim enhancing carcinomas exhibited central necrosis.[37]

Unfortunately, false negative finding of palpable breast mass in MG have been estimated at between 4% and 12%.[38,39] Therefore, malignancy cannot be excluded. For this, ultrasonography is used as an adjunct to MG to further evaluate palpable masses, especially in women with mammographically dense breast (Sachin P.N at al. 2007).[24]

From proven literatures, MG and USG are well established diagnostic modalities for the breast. They have high diagnostic yield, but not having 100% sensitive and specific. [40,41] But, if MG is combined with USG then they can obtain very significant progress in sensitivity and specificity for detecting different breast lesions and is supported by this study (Tiwari et al. 2017).[25] The patients with symptoms have also been studied previously with the combination of MG and USG imaging in Moss et al.[42] reported sensitivity of 99.2% in 368 patients.; Shetty MK and Shah YP[43] reported a sensitive 100%. Their findings are comparable with present finding sensitive of 100% in case of malignant lesion and case detection rate of 97% in benign lesions.[25] It was also stated from this study that the combination of these two non-invasive procedures (MG+USG) can almost achieve the accuracy of FNAC in detecting breast malignancy (Tiwari et al. 2017).[25]

The overall cancer detection sensitivity of MG was 47.4%; 60% in fatty breast and 42.9% in dense breast (yoonsoo kim et al. 2018.)[44] It showed that MG has less diagnostic accuracy in dense breast for which USG is a supplemental tool for breast cancer detection.

This evidence-based study in detecting breast cancer showed the sensitivity and specificity of MG reports were 73% and 45% and in USG was 69% and 49% respectively (Akbari ME etal. 2010).[26] These indices

varied in different studies (Berg et al., 2008; Prasad et al., 2007; Devolli –Disha et al., 2009; Akbari etal., 2010).[3,24,26,45] Different values of MG and USG in sensitivity and specificity were due to factors affecting in reporting are given (Prasad et al. 2007).[24]

The significant difference in sensitivity and specificity of MG and USG were absent between two types of radiological reports. But, there were significant difference in these indices with international reports due to effect of different type of risk factors. The main factors are manpower and quality of machine and their setting which for standard policies and guidelines are must to follow (Akbari et al. 2012).[26]

ABVS with mammography is significantly better than mammography alone for detecting breast cancer, especially for dense-breasted women. These women have higher risk of developing breast cancer with less likely to have cancer detection by standard mammography screening (Kelly KM at al. 2010).[27]

Cancer detection with ABVS may improve with reader experience and possibly a CAD system. In addition to this, the availability of previous comparative studies might have contributed to better sensitivity and fewer recalls. Assuming that many of the ABVS "missed" cancer could be potentially be avoided, ABVS with MG could have sensitivity approaching 95%. This might be comparable to the sensitivity of MRI, but at a fraction of the cost (Kelly KM at al. 2010).[27]

Invasive cancers detection by ABVS was 90% smaller than 20mm where BCSC detected 71% of less than 20mm (Kelly KM et al. 2010).[27] The smaller size of invasive cancers detected by combined ABVS to MG suggests that this technology may have the potentiality in impacting breast cancer survival and treatment options, though this has not yet been shown (Kelly KM et al. 2010).[27]

The sensitivity of ABVS and MG were 67% and 40% respectively. The combined effect of overall diagnostic sensitivity was nearly 90% in breast cancer detection. Significant small size invasive tumors were detected by ABVS; 14 out of 21 ($p=0.006$) or 67% of cancers less than 10mm or less were detected only by ABVS and not evident by mammography (Kelly KM et al. 2010).[27] The sensitivity for this tumors was 81% compared with 33% for MG. Cancer detection for invasive tumors measuring 11 to 20 mm increased from 8 to 14 with the addition of ABVS (Kelly KM et al., 2010).[27]

For women with dense breast, ABVS detected 65% compared with 39% mammography alone ($p=0.02$). Addition of ABVS to MG more than doubled cancer detection from 19 to 39(Kelly KM et al., 2010).[27] ABVS resulted in more recalls for additional imaging than MG ($p<0.001$). Recalls were 4.2% for screening MG and 7.2% for ABVS. Recalls increased from 4.2% to 9.6% adding ABVS to MG. Specificity based on recalls was 89.9% for ABVS and 95.15% for MG but for combined recalls for ABVS and MG were 98.7 %(Kelly KM et al. 2010).[27]

CONCLUSION

ABVS has a high diagnostic accuracy, better lesions size detection, operator –independent and an alternate to mammographically contraindicated women. ABVS with MG is significantly better than MG alone for detecting breast cancer, especially for dense breast women because these women have high risk of developing breast cancer where MG screening has less likely to detect cancer. ABVS with MG could have

sensitivity approaching 95% which may be comparable to the sensitivity of MRI. The combination of ABVS and MG can also detect the smaller size of invasive cancer and have potential to impact breast cancer survival and treatment option by staging although ABVS alone has more recalls for additional imaging than MG.

Cancer detection is higher in ABVS group than conventional USG although absolute value was little different. This ABVS is also called a good supplemental tool for MG when screening for breast cancer in a large population. The detection of breast cancer size is better with ABVS than conventional USG but in case of invasive cancer they are almost nearly equal in mean size detection. So, ABVS shows comparable diagnostic performance when compared with conventional USG but the combination of ABVS and USG gives better result than single in either with symptoms or without symptoms of women.

In case of benign such as fibroadenoma, ultrasonography diagnosed 100% where MG diagnosed 68% but the combined effect will be equal to ultrasonography finding 100%. It is also known that USG is the investigation of choice in palpable mobile breast lesion. The diagnosis of cystic breast lesion by USG is 100% whereas MG detects only 33%.

With the malignant lesions, USG diagnosis is more accurate than MG but combination of both modalities diagnosed 100%. The greater accuracy of USG in the diagnosis of false negative mammographic finding has proved its importance as an adjunct to MG in preoperative assessment of breast lesion.

S.R.C Benson et al.[36] also concluded that USG is better than MG for detection of invasive breast cancer and the combination of USG and MG is better than either modality. This combination of non-invasive procedures can almost achieve the accuracy of FNAC in detection of breast malignancy.

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