Original Article

Evaluation of high-risk patients with dense breast on high-resolution ultrasound for screening and detection of breast cancer where mammography is of low significance

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Abstract

Background: Early diagnosis of breast cancer is a challenging problem in high-risk patients with dense breast. The risk of breast cancer is many fold higher in dense breast as compared to nondense on one side with limited screening or diagnostic role of mammography on the other side. The aim of our study is to elaborate the role of high-resolution ultrasonography (HR-USG) as adjunct modality to overcome this limitation.

Materials and Methods: This is a prospective observational study conducted in the breast care clinic of a tertiary care cancer hospital. Totally, 2720 patients were enrolled for mammography. Out of these, 339 patients were reported according to Breast Imaging Reporting and Data System (BIRADS) as 0 (inconclusive) and were suggested for further evaluation by other modalities. All patients reported for mammography as BIRADS 0, were included in this study for HR-USG.

Results: On HR-USG, 33.4% of patients with dense breast were shown to have suspicious (BIRADS 5) lesions. 21.7% had simple cysts. Fibro adenomas and abscess were seen in 18% and in 15% of patients, respectively. Other findings were duct ectasia (4.3%) and galactocele (3.4%). 1.4% of patients were normal on HR-USG.

Conclusion: Our study showed HR-USG as a modality of choice that supersedes the diagnostic efficiency of mammography in patients with dense breasts thus enhances early detection and better treatment of breast cancer, decreasing mortality owning to delay in diagnosis.

Keywords: Breast cancer, Breast Imaging Reporting and Data System, dense breast, early detection, high-resolution ultrasound, mammography

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INTRODUCTION

The role of mammography in early detection of breast cancer is emphasized worldwide but has limitations in case of dense breasts. Rate of false-negative mammography is 10%–15% which is increased to >60%–80% in case of dense breast with very poor sensitivity to detect lesions and high risk for missing lesion.[1]

Density does not affect the diagnostic sensitivity of HR-USG on the one hand and is cost-effective on the other

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hand.[2] The technological advancement of sonographic devices helps to have precise characteristics of lesion. Hence, HR USG might be used as an adjunct modality of choice for dense breasts.

MATERIALS AND METHODS

The study was conducted from January 2018 to December 2020 at breast care clinic of a tertiary care hospital in a developing country that is the only breast care clinic in public sector of that region covering the population of approximately 50 million in total and 52% of this is females. 2720 patients presented for digital mammography with standard views of craniocaudal and mediolateral oblique views either for screening or with different presenting complaints were enrolled. The mean age of presentation was 40 years with standard deviation of 6.8 years. 339 constituting 12.5% of total mammograms were reported as dense mammograms and categorized as Breast Imaging Reporting and Data System (BIRADS) 0. All patients with dense mammogram were included in study and HR-USG, in supine position with arms raised to head using high-frequency probe of 8 MHz moving in spoke wheel pattern keeping probe in both transverse and longitudinal directions, was added to all these mammograms. Patients who were previously diagnosed cases of carcinoma breast and those who refused for HR-USG were excluded from the study.

RESULTS

The most common presentation of patients was lump in either breast. Other complaints included pain/mastalgia, nipple discharge. Only three patients underwent mammography for screening purpose [Table 1].

The frequency of lesions based on BIRADS grading on HR-USG is shown in Figure 1.

Lesions were characterized on the basis of different features including (1) shape of lesion, round, oval, or irregular, (2) orientation of lesion, wider than taller, or taller than wider, (3) margins, regular, lobulated or irregular, well-circumscribed, or ill-defined, (4) echogenicity of lesion, hypoechoic, isoechoic, hyperechoic, or anechoic, (5) posterior acoustic enhancement or posterior shadowing, (6) calcifications, and (7) axillary lymph nodes. The frequency of different breast lesions on HR-USG in patients reported as BIRADS 0 on mammography is shown in Figure 2.

Table 1: Frequency of different presenting complaints

Presenting complaints	Total, *n* (%)
Nipple discharge	16 (4.8)
Pain	62 (18.3)
Lump right breast	118 (34.82)
Lump lefty breast	107 (31.5)
Lump both breast	30 (8.8)
Inverted nipples	3 (0.89)
No complaints/screening	3 (0.89)

Ninety-one (27%) patients were labeled as BIRADS 4 while 113 (33.4%) patients as BIRADS 5. USG-guided Trucut biopsies were done in all BIRADS 4 and 5 lesions (204 patients). Histopathology of 200 (98.2%) confirmed those carcinomas while inflammatory lesions were reported in 4 (1.8%) cases. mammogram (a) and HR-USG of the same patient (b) showing missed lesion of BIRADS 5 on mammography later detected on HR-USG and was confirmed as intraductal carcinoma on histopathology of Trucut biopsy [Figure 3a and b].

DISCUSSION

Breast cancer is the most common female cancer in the world with the highest cancer-related mortality rate in developing countries.[3] The major factors for this high mortality include failure of early detection due to lack of awareness and screening programs and lack of resources for diagnostic facilities in developing countries.[3] Early detection is the only weapon to fight against this high mortality rate.[4] Thus, patients presenting with any breast lesion or complaints need proper evaluation.[5] Triple assessment including clinical examination, imaging, and fine-needle aspiration or core biopsy has established a role for breast lesions evaluation.[5,6]

Clinical examination alone is insufficient but mammography alone or in combination with clinical examination has a commendable role to enhance early detection of breast

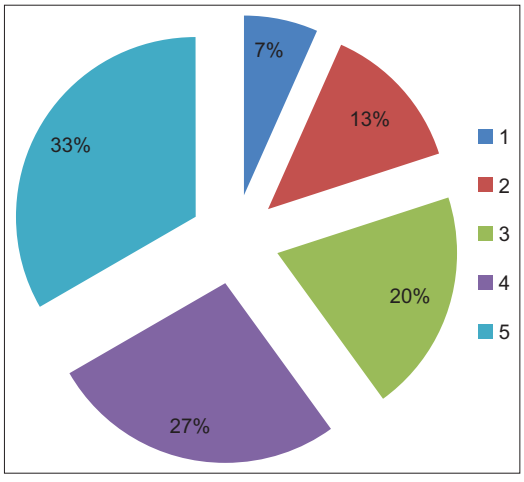

Figure 1: Breast Imaging Reporting and Data System (BIRADS) grading on HR-USG where mammogram was graded as BIRADS 0

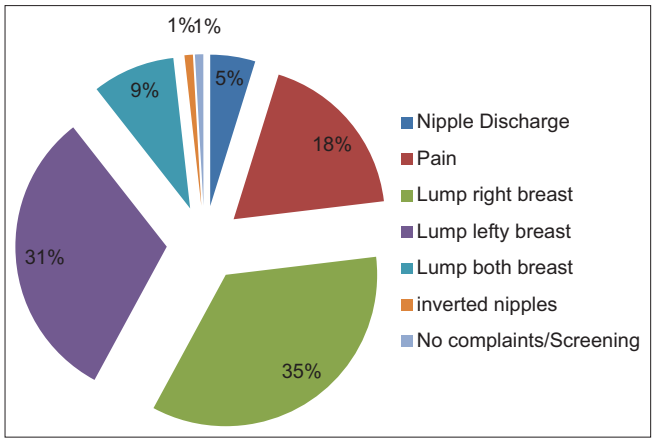

Figure 2: Frequency of different breast lesions on HR-USG in patients with Breast Imaging Reporting and Data System 0 on mammogram

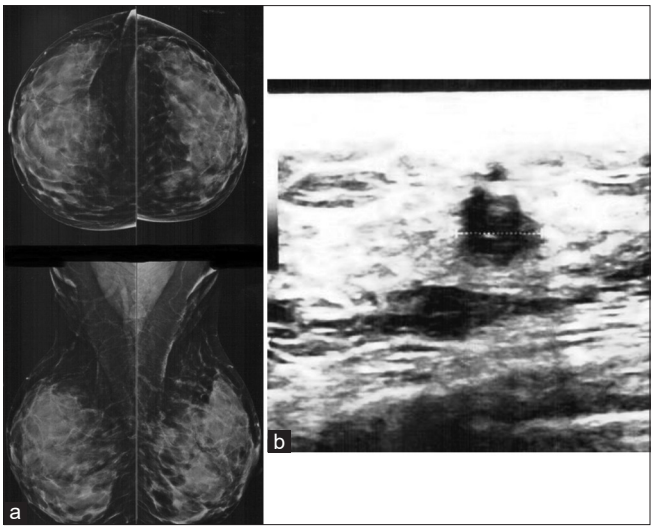

Figure 3: (a) Dense mammogram obscuring underlying lesion (b) HR-USG of the same patient shows Breast Imaging Reporting and Data System 5 lesion in upper outer quadrant of the right breast that was proven carcinoma on histopathology of Trucut biopsy

cancer.[7] This early diagnosis might be further enhanced by adding other modalities to mammography that would help to detect those small lesions which are missed on mammography in case of dense breast.

Mammography has a major contribution to decreasing the breast cancer-related mortality by enhancing the early detection of lesion through mass screening programs in developed countries. Health organizations recommend screening mammography in low-risk patients after the age of 40 years but in high-risk patients after 35 years with no age restriction for diagnostic purpose in clinically symptomatic patients presenting with lumps.[8] Little or no screening role of mammography is already known in young patients due to high tissue density at a young age that decreases its sensitivity for lesion detection. On the other hand, more and more cases of breast cancer are being reported at younger age, and estimated 6.6% of total breast cancers are diagnosed in young women below the age of 40 years.[9] Overall sensitivity of mammography for the detection of small lesion (up to 2 cm)[10] is around 85% which falls to 47.8%–64.4% in case of dense breast.[11] Poor sensitivity for detection of lesion in dense breast renders these patients to present later on with breast cancer in late stage thus increasing mortality.

Breast lesions on mammography are reported on BIRADS scale on the basis of susceptibility of lesion for malignancy. Breast lesion is graded on BIRADS scale as 0, 1, 2, 3, 4, and 5 for inconclusive study, normal, benign, probably benign, probably suspicious, and highly suspicious lesions, respectively. If the patient is already biopsy-proven known case of malignancy, lesion is graded as BIRADS 6.

Dense breast tissue refers to the appearance of a mammogram. Density on mammogram is determined by the ratio of nondense tissue to dense tissue. Breast tissue is composed of milk glands, milk ducts and supportive tissue (dense breast tissue), and fatty tissue (nondense breast tissue). When viewed on a mammogram, women with dense breasts have more dense tissue than fatty tissue.

On a mammogram, nondense breast tissue appears dark and transparent. Dense breast tissue appears as a white area on a mammogram, which makes it difficult to see through.

Levels of density are described according to BIRADS. The levels of density are often recorded in mammogram reports using letters A, B, C, and D. Fourth Edition of BIRADS guidelines describes the levels of density as – A: Almost entirely fatty (≤25% dense tissue), B: Scattered areas of fibro glandular density (25%–50% dense tissue), C: Heterogeneously dense (50%–74% dense tissue), D: Extremely dense (≥75% dense tissue) indicates that nearly all of the breast tissue is dense.[12] The fifth Edition of BIRADS guidelines removed the percentage system and emphasized on masking effect of dense tissue. According to these new guidelines, a mammogram could be dense even if glandular tissue is <50%, but the concern is about an area of dense tissue that could potentially be masking an underlying cancer. All this provides freedom to individual reporting radiologist to classify breast density in more meaningful way.[13]

Breast tissue density has geographic and ethnic variations.[14] High-breast density is common in young women before menopause or below the age of 40 years. Our patients with dense mammograms ranged between 35 and 53 years.

Other factors increasing tissue density include lactation and hormone replacement therapy and low body mass index (BMI). With advancing age, increasing parity and high BMI the tissue density are reduced.[15-17] About 40% of all women are estimated to have heterogeneously dense breasts, and 10% are estimated to have extremely dense breasts.[18] Poor sensitivity of mammogram for detection of small lesion in dense breast leads to failure of early detection of breast cancers.

A high density of breast tissue is one of the strong predictors for breast cancer as studies have shown that the risk of breast cancer increases by four to six folds in dense breast as compared to nondense breasts.[1] A high density of breast has been shown to be related to larger size breast cancers with positive lymph nodes and also with cancers diagnosed other than screening programs. It might be due to poor accuracy of mammography to detect lesions in dense breast so small tumors can easily be missed on mammography thus causing failure for early detection. These patients might present later on with clinically palpable mass. Increased risk for breast cancer in patients with high-breast density has been shown to be related to factors other than poor detection. However, masking effect of tissue density on screening mammography is a foremost cause of late presentation of breast carcinoma in dense breast thus is the prime cause for high mortality rate in these patients. These pitfalls can be overcome by adding other modalities to mammography for dense breast so that lesion missed on mammography might be picked on other modalities.[5]

Breast density is a big barrier to the early detection of any breast lesion on mammography.[19] Breast cancers diagnosed in dense breasts are usually in locally advanced stage or high T stage with positive nodes.[20] More over incidence of interval cancers in dense breast is 18 times higher and shows worse prognosis.[21] High risk of breast cancer in dense breast is another aided factor to this reduced mammographic sensitivity emphasizing for evaluation of patients by multimodality approach.[22]

The American College of Radiology BIRADS Atlas first described and standardized the breast density based on the relative ratio of glandular tissue to fatty tissue with subsequent modification over the years.[23] A numeric percentage of breast tissue with reference to categories 1–4 has been recommended in Fourth Edition published in 2003.[11,13] Although the latest edition has removed numeric percentages to describe density, it is yet widely used.

At present, no specific guidelines are there for screening of dense breast. However, research studies are being conducted in an attempt to find any improved detection sensitivity by a combination of modalities.[24] High screening and diagnostic sensitivity by supplementing mammogram with HR USG as compared to mammogram alone have been shown in a retrospective study.[24] The addition of other modalities including magnetic resonance imaging (MRI) and HR-USG is recommended in different studies.[18]

MRI is used as a supplement tool with mammography or USG for breast cancer screening.[25] MRI is extensively used and highly recommended as a supplemental modality for high-risk patients, especially with dense breast. The European Society of Breast Imaging, the European Society of Breast Cancer Specialists, and the American Cancer Society all have recommended MRI for screening of high-risk patients.[26] Breast MRI is thought to be an effective modality to improve the sensitivity for screening breast cancer with mammography alone.[18] Intravenous contrast (gadolinium) is administered for MRI breast that is not limited by high tissue density. However, MRI is not well practiced in developing countries because of cost-effect. The number of true-positive test results is increased by MRI; on the other hand, the potential risk of increasing the rate of false-positive findings and unnecessary biopsies and treatments is increased. Failure to pick microcalcifications and high false-positive results leading to more biopsies than other investigations are the limitations of MRI.

Furthermore, MRI is an expensive and complicated imaging. Most patients cannot tolerate to stay in magnet for a long time of up to 20 min. The financial status of our Population is below average. Moreover, a poor literacy rate hinders their counseling for this complicated lengthy procedure. Truncated MRI with short period study could be a solution for this issue, but not much data are available to support this. A few trails are published showing no difference in lesion detection between MRI with standard protocol or truncated protocols.[27,28] Hence, truncated MRI might be used in future as alternate screening tool to avoid underdiagnosis or interval cancer rates in dense breast.

The HR-USG is another more reliable modality as an adjunct to mammography for the detection of small lesions in dense breast those are missed on mammography.[29] We used HR USG as an adjunct modality for high-risk patients with dense breasts because a large number of our patients belong to low-income group and high cost of MRI is not affordable by them. The combined modalities of mammography and HR USG increase the sensitivity for early detection of breast cancers as shown in our study [Figure 3a and b]. Hence, HR-USG is a modality

of choice as an adjunct technique for dense breast in developing couturiers for screening of high-risk patients with high breast tissue density.

CONCLUSION

Mammography has poor sensitivity for the detection of lesion in dense breast which limits its contribution to screening or diagnosis in such cases. HR-USG as an adjunct modality overcomes this limitation and enhances early detection of breast cancers thus reducing the mortality rate on account of delay in diagnosis. Hence, it is a modality of choice for developing countries where MRI is not in practice due to its cost effect and complexity of procedure.

Limitation of study

It is a hospital-based study where most of the presenting patients are symptomatic with only few for screening purpose. A broad population-based or multi-centric study based on a comparison of HR USG with MRI is required to complete the debate on the supremacy of HR USG on mammography and MRI for screening and early detection of breast cancer in dense breasts.

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Conflicts of interest

There are no conflicts of interest.

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