Original Article

Radiology Section

Efficacy of Spectral Doppler Indices in Predicting Malignancy in BI-RADS 3 Breast Lesions: A Prospective Cohort Study

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ABSTRACT

Introduction: Breast Imaging, Reporting and Data System (BI-RADS) is an effective tool for management of patients with breast pathologies. While the BI-RADS 1 (negative) and BI-RADS 2 (benign) categories patients are advised for routine mammography screening. BI-RADS 4 (suspicious abnormality) and BI-RADS 5 (highly suggestive of malignancy) categories patients are recommended for tissue diagnosis, BI-RADS 3 category patients are managed with follow-up examinations. But upto 2% of BI-RADS 3 lesions are proved to be malignant on follow-up examinations and tissue diagnosis.

Aim: To evaluate the efficacy of spectral Doppler indices in predicting malignancy in BI-RADS 3 category breast lesions.

Materials and Methods: A prospective cohort study was conducted in the Department of Radiology, Katuri Medical College, Guntur, Andra Pradesh, India from July 2019 to February 2021. Study was conducted on 292 BI-RADS 3 lesions from 257 patients to evaluate the efficacy of spectral Doppler indices in differentiating malignant BI-RADS 3 lesions from benign ones. All the breast masses were evaluated with spectral doppler and the resistive and pulsatility indices were compared with histopathology findings of the suspicious lesions detected in follow-up examinations. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 2017 version 25, and the quantitative data was expressed in mean and standard deviation.

Results: The patients recruited in the study were in age range of 27-80 years, and the mean age of the patients was 46±15 years (mean±SD). Follow-up examinations and tissue diagnosis of suspicious lesions revealed 8 out of 292 BI-RADS breast masses to be malignant. On spectral Doppler analysis, high resistivity and pulsatility indices are predictive of malignancy. A resistive index of more than 0.6 as a sign of malignancy proved to have a sensitivity of 87.5% and specificity of 85.5% and more than 0.8 as a sign of malignancy has a sensitivity of 25% and specificity of 95%. A pulsatility index of more than 0.9 as a sign of malignancy has a sensitivity of 87.5% and specificity of 87% and more than 1.6 as a sign of malignancy has a sensitivity of 37.5% and specificity of 96%.

Conclusion: Spectral doppler is reliable in the prediction of malignancy of BI-RADS 3 breast masses.

Keywords: Breast imaging, Breast carcinoma, Colour and spectral doppler, Diagnostic ultrasound, Reporting and data system 3 breast masses

INTRODUCTION

Breast malignancy is one of the most common causes of cancer deaths in females, and its incidence has been steadily increasing over the last a few decades [1]. In the late 1980s, American College of Radiology (ACR) provided a standardised breast imaging lexicon and classification system for mammography [2]. Later ACR added ultrasound and Magnetic Resonance Imaging (MRI) guidelines to existing BI-RADS mammography classification [Table/Fig-1] [3].

According to BI-RADS, category 1 and 2 patients need routine mammography screening, whereas category 4 and 5 patients are recommended for tissue diagnosis and further management on the basis of the histopathology reports. But patients with BI-RADS 3 masses are managed with follow-up examinations. Upto 2% of these BI-RADS 3 lesions are proved to be malignant on follow-up examinations [3]. Some of these patients even presented with advanced disease on follow-ups. Hence, an effective diagnostic tool to predict malignancy of BI-RADS 3 breast masses is a great necessity.

It is an established fact that malignant lesions are characterised by high cell turn over and neoangiogenesis [4]. Colour and spectral doppler can effectively demonstrate neovascularity and characteristics of vascular flow [5,6]. So, in the present study, authors evaluated the efficacy of spectral Doppler to evaluate the changes in the characteristic of vascular flow in the intra-lesional vessels of BI-RADS 3 lesions to predict malignancy. To the best

Assessment	Management	Likelihood of Cancer
Category 0: Incomplete- Need additional imaging evaluation and/or prior mammograms for comparison	Recall for additional imaging and/or comparison with prior examination(s)	N/A
Category 1: Negative	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 3: Probably benign	Short-interval (6-month) follow-up or continued surveillance mammography	>0% but ≤2% likelihood of malignancy
Category 4: Suspicious Category 4A: Low suspicion for malignancy Category 4B: Moderate suspicion for malignancy Category 4C: High suspicion for malignancy	Tissue diagnosis	>2% but <95% likelihood of malignancy >2% to ≤10% likelihood of malignancy >10% to ≤50% likelihood of malignancy >50% to <95% likelihood of malignancy
Category 5: Highly suggestive of malignancy	Tissue diagnosis	≥95% likelihood of malignancy
Category 6: Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

[Table/Fig-1]: BI-RADS assessment categories with management recommendations [3].

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of our knowledge, this is the first study that evaluates the role of spectral doppler in BI-RADS 3 lesions.

MATERIALS AND METHODS

A prospective cohort study was conducted at the Department of Radiology, Katuri Medical College, Guntur, Andra Pradesh, India from July 2019 to February 2021. This study was approved by our institutional review board. The last patient was recruited in February 2020.

Sample size calculation: Open-epi software was used to calculate sample size. Sample size required to conduct the study was 267 for precision of 6% and 384 for precision of 5%. A total of 330 female patients with 390 lesions were recruited but only 257 cases with 292 lesions turned up for follow-up.

Inclusion and Exclusion criteria: All the patients with BI-RADS 3 breast lesions showing atleast single arterial signal were included in the study and the patients lost on follow-up and unwilling for tissue diagnosis on follow-up examinations were excluded from the study.

Procedure

All examinations were performed by one experienced radiologist. A detailed informed consent was obtained from the patients before performing B-mode grey scale examination of both breasts followed by spectral Doppler of the masses using 5-10 MHZ probe of GE LOGIC P5 ultrasound machine. Colour window was optimised to visualise small caliber, low velocity vessels and spectral Doppler tracings of all of the visualised vessels were obtained. Where the lesions showed more than one arterial signal mean Resistive Index (RI) and Pulsatility Index (PI) were taken into calculations. The patients were advised for follow-up scans at 6 and 12 months. The lesions that showed suspicious changes on the follow-up examinations were subjected to tissue diagnosis, and the resistive

and pulsatility indices of spectral doppler were compared with histopathology findings.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS 2017 version 25, and the quantitative data was expressed in mean and Standard Deviation (SD). Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were obtained.

RESULTS

The patients recruited in the study were in age range of 27-80 years, and the mean age of the patients was 46±15 years. Out of 257 patients, 17 patients presented with two breast masses, six patients with three breast masses and two patients with four breast masses. Follow-up scans and tissue diagnosis of the lesions with suspicious changes revealed 8 out of 292 lesions to be malignant. Out of the eight lesions, three were diagnosed to be malignant at six months follow-up and remaining 5 at 12 months follow-up. The spectral Doppler findings were compared with the histopathology findings [Table/Fig-2].

The mean resistive index of the malignant lesions was 0.73±0.11. Out of eight malignant masses proved on tissue diagnosis, seven masses showed RI more than 0.6 with sensitivity of 87.5% and specificity of 85.5% for prediction of malignancy [Table/Fig-2-4]. Only two out of eight malignant masses showed RI more than 0.8 with sensitivity of 25% and specificity of 95%.

The mean pulsatility index of the malignant lesions was 1.35±.0.43. Of the 292 lesions 44 lesions had pulsatility index more than 0.9, and 7 out of these 41 masses were malignant with sensitivity and specificity of 87.5% and 87% respectively [Table/Fig-5,6]. Similarly, the pulsatility index more than 1.6 as the criteria of malignancy had sensitivity and specificity of 37.5 and 96%, respectively with false positives of 11 [Table/Fig-2].

Index		True positives A	False negatives B	False positives C	True negatives D	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Resistive index	>0.6	7	1	41	243	87.5	85.5	14.6	99.5
	>0.7	5	3	26	258	62.5	90.8	16	99
	>0.8	2	6	14	270	25	95	12.5	98
Pulsatility index	>0.9	7	1	37	247	87.5	87	15.9	99.5
	>1.2	4	4	22	262	50	92.25	15.3	98.5
	>1.6	3	5	11	273	37.5	96	21.5	98

[Table/Fig-2]: Comparison of spectral Doppler findings with the histopathology findings.
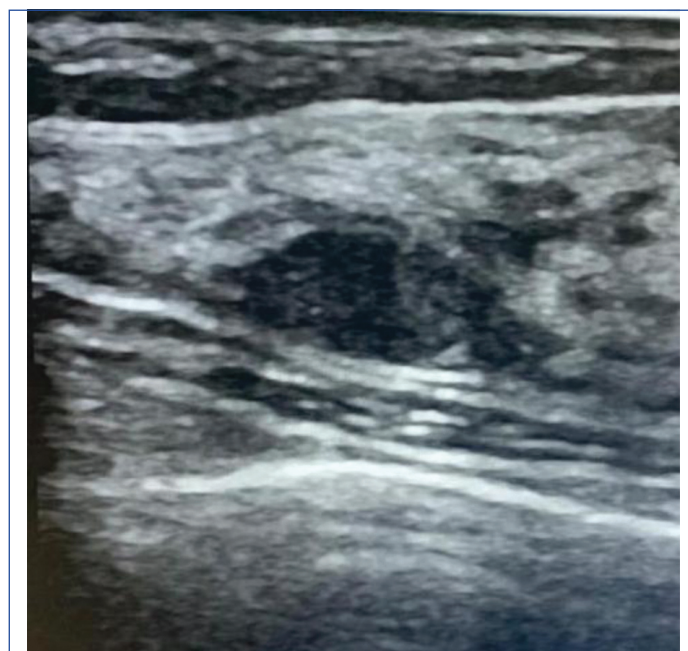

[Table/Fig-3]: Palpable mass lesion in the left breast of a 32-year-old woman. The grey scale B-mode image demonstrates a BI-RADS 3 lesion.
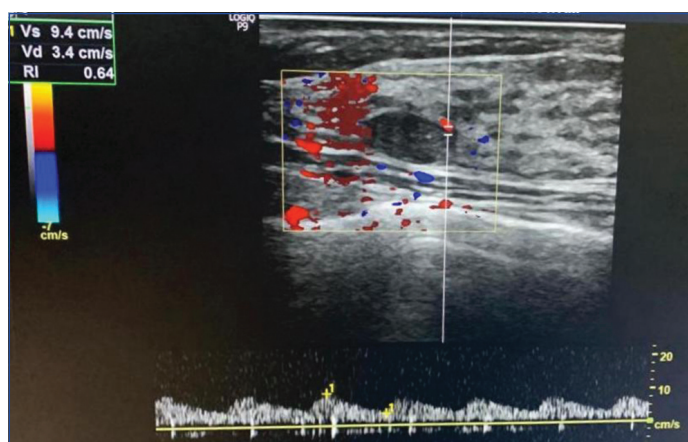

[Table/Fig-4]: BI-RADS 3 lesion showing resistive index of 0.64.

DISCUSSION

The present study revealed that resistivity and pulsatility indices were significantly higher in malignant BI-RADS 3 lesions than benign ones. Comparison of histological findings with various cut off points of RI as signs of malignancy revealed that RI value more than 0.6 has reliable sensitivity of 87.5% and specificity of 85.5% and PI value more than 0.9 has reliable sensitivity 87.5% and specificity of 87%.
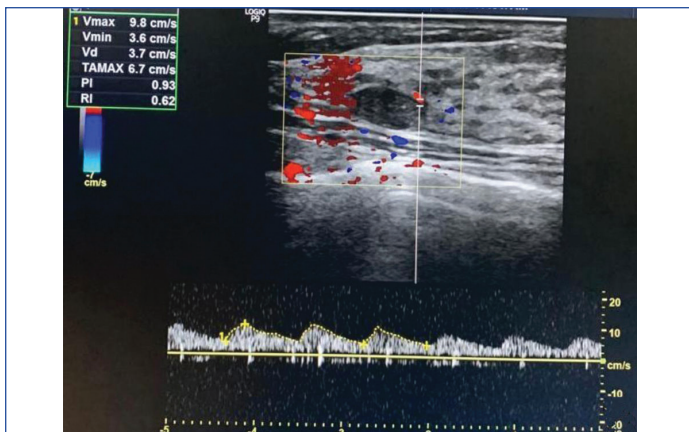
[Table/Fig-5]: Colour and spectral doppler of the same lesion as of [Table/Fig-3] shows high Resistive index (>0.6) and Pulsatility index (>0.9).
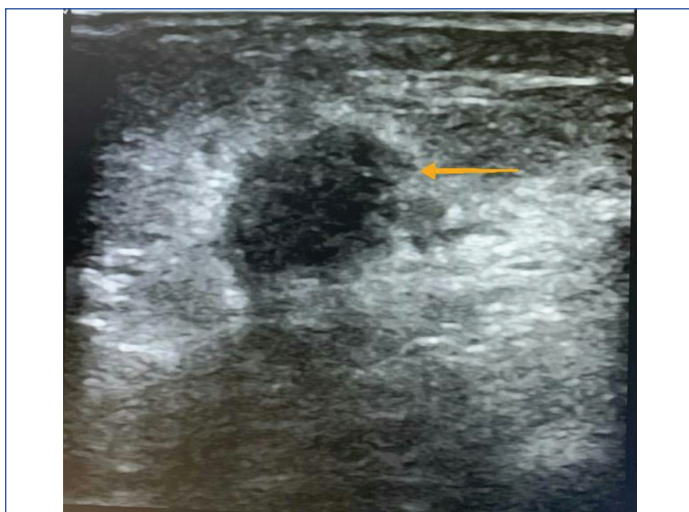
[Table/Fig-6]: Follow-up diagnostic ultrasound of the same patient as of [Table/Fig-3] revealed suspicious changes (Arrow pointed to spiculated margins). The tissue diagnosis proved malignancy.

According to present study, when we considered an RI value more than 0.6 as a sign of malignancy, 48 masses needed immediate tissue diagnosis, and seven out of these 48 lesions were proven malignant with positive predictive value of 14.6%. In other terms, BI-RADS 3 lesions with RI more than 0.6 can be considered BI-RADS 4 lesions and recommended for immediate tissue diagnosis. Likewise, if we considered a pulsatility index value more than 0.9 as a sign of malignancy, 44 lesions would be considered BI-RADS 4 lesions, and immediate tissue sampling would prove seven out of these 44 lesions malignant with positive predictive value of 15.9%.

Since, this is the first study conducted exclusively on BI-RADS 3 lesions, we could only compare our study results with the series that evaluated role of spectral Doppler in breast malignancies. Sirous M et al., in a prospective study evaluated 1110 breast masses using power Doppler sonography over a period of 3 years, concluded

that RI value of 0.64 had sensitivity of 88% and specificity of 59%, and PI value of 0.9 had sensitivity of 89% and specificity of 51% for prediction of malignancy. The mean RI and PI of malignant breast masses were 0.78±0.23 and 1.49±0.51, respectively [7].

Keshavarz E et al., conducted analytic cross sectional study on 100 breast masses and found that RI more than 0.68 had sensitivity of 85% and specificity of 74%, and PI more than 0.93 had sensitivity of 90% and specificity of 85.7% for prediction of malignancy. The mean RI and PI values of malignant lesions in their study were 0.73 and 1.09, respectively [8]. In the present study, the sensitivity of RI and PI values more than 0.6 and 0.9 as the signs of malignancy were 87.5% and correlated with the above two studies. However, the specificity of RI and PI more than 0.6 and 0.9 as the signs of malignancy are 85.5% and 87% in the present study. But the Sirous M et al., study reported them to be 59% and 51% respectively and Keshavarz E et al., study reported them to be 74% and 85.7% respectively [7,8].

Limitation(s)

Only the lesions that showed suspicious changes on follow-up examinations were subjected to the tissue diagnosis. The fate of the lesions that had not shown detectable changes on follow-up examinations remains unknown. Also, follow-up evaluations beyond 12 months were not performed.

CONCLUSION(S)

This prospective study proves that Resistivity and Pulsatility indices on spectral Doppler of BI-RADS 3 category breast masses have good association with histopathology findings. BI-RADS 3 breast masses with high RI (0.6) and PI (0.9) need to be escalated from BI-RADS 3 category to BI-RADS 4 category and recommended for immediate tissue diagnosis.

REFERENCES

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61(2):69-90. Doi: 10.3322/caac.20107. Epub 2011 Feb 4. Erratum in: CA Cancer J Clin. 2011;61(2):134. PMID: 21296855.

[2] American College of Radiology. Breast Imaging Reporting and Data System® (BI-RADS®) Reston, Va: American College of Radiology; 1992. [Google Scholar].

[3] D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA, et al. ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. Reston, VA, American College of Radiology; 2013.

[4] Folkman J, Watson K, Ingber D, Hanahan D. Induction of angiogenesis during the transition from hyperplasia to neoplasia. Nature. 1989;339(6219):58-61. Doi: 10.1038/339058a0. PMID: 2469964.

[5] Ramos I, Fernandez LA, Morse SS, Fortune KL, Taylor KJ. Detection of neovascular signals in a 3 day Walker 256 rat carcinoma by CW Doppler ultrasound. Ultrasound Med Biol. 1988;14(2):123-26. Doi: 10.1016/0301-5629(88)90179-2. PMID: 2450420.

[6] Taylor KJ, Ramos I, Carter D, Morse SS, Snower D, Fortune K. Correlation of Doppler US tumor signals with neovascular morphologic features. Radiology. 1988;166(1 Pt 1):57-62. Doi: 10.1148/radiology.166.1.2447604. PMID: 2447604.

[7] Sirous M, Sirous R, Nejad FK, Rabeie E, Mansouri M. Evaluation of different aspects of power Doppler sonography in differentiating and prognostication of breast masses. J Res Med Sci. 2015;20(2):133-39. PMCID: PMC4400706.

[8] Keshavarz E, ZareMehrjardi M, Karimi MA, Valian N, Kalantari M, Valian M, et al. Diagnostic value of spectral doppler ultrasound in detecting breast malignancies: An original article. Int J Cancer Manag. 2018;11(2):e8200. Doi: 10.5812/ijcm.8200.

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