

DIAGNOSTIC ACCURACY OF RESISTIVE INDEX MEASURED THROUGH COLOUR DOPPLER ULTRASOUND OF THE BREAST LUMPS FOR DIAGNOSING BREAST CANCER KEEPING HISTOPATHOLOGY AS A GOLD STANDARD

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ABSTRACT

OBJECTIVES: To determine diagnostic accuracy of resistive index measured through colour Doppler ultrasound of the breast lumps for diagnosing breast cancer keeping histopathology as a gold standard. **STUDY DESIGN:** Cross sectional validation study. **SETTING:** Department of radiology Quaid-e-Azam international hospital islamabad from 11-02-2021 to 10-08-2021. **METHODOLOGY:** A total of 215 patients were included in this study. In all the patients breast lumps were examined by ultrasonography on Grey scale using Xario200 Toshiba ultrasound machine with high linear probe frequency probe of 11MHz. Then with the same probe Doppler ultrasound of the lesion was performed using either colour or power Doppler. **RESULTS:** Overall sensitivity, specificity and diagnostic accuracy of Resistive Index was 86.7%, 78.9% and 86.0%, respectively. Positive predictive value and negative predictive value of Resistive Index was 97.7% and 36.6%, respectively. **CONCLUSION:** This study proves diagnostic accuracy of resistance index measured through colour Doppler ultrasound of the breast lumps for diagnosing breast cancer in patients avoiding the need for biopsy.

Key words: Breast cancer, Breast lumps, Resistive index

Introduction

Breast cancer is considered the leading cause of cancer associated deaths¹ especially in the developing countries like Pakistan. A study conducted by Fitzmaurice C in year 2018 systematic analysis for the global burden of disease study for 32 cancer groups from 1990 to 2015 showed 2.1 million new cases were reported, with 627,000 deaths.^{2,3} One in every nine Pakistani women has have life time risk of being diagnosed with breast malignancy.⁴ By reason of many misconceptions and low socioeconomic status there is low rate of early detection and majority of patient often present at advance stage of disease. The best cure for treatment of breast carcinoma lies

in its early diagnosis and prompt management. In a study conducted by International Agency of Research on Cancer in 2018 report showed incidence of 34,066 cases of breast cancer had been reported in Pakistani women.⁵ Due to late diagnosis and referral of patient the mortality rate of breast carcinoma is high. If diagnosis is done at an early stage of disease, chances of survival and recovery are much high as compared to later stages, thus, itsutmost important to spread alertness about the early diagnosis and early management of breast cancer among the general community.^{6,7}

Tumors are graded as low grade (G1), intermediate

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grade (G2) and high grade (G3) by noting ham criteria.² Tumors staging is done according to American joint committee on cancer T classification T1 < 2cms, T2 > 2cms, T3 > 5cms, T4 is excluded due to missing data due to tumor invasion to surrounding structures.

Mammography, ultrasound, CT, MRI and scinti mammography are used for the evaluation of breast cancer. Diagnostic accuracy of mammography to diagnose malignant breast lesions keeping histopathology as gold strand is upto 89.3%.⁸ However, with the use of imaging modality further improves it to reliably differentiate between benign and malignant breast lesions. Ultrasound is used as an adjunct to the mammography for screening of the malignant breast nodules.¹

Malignant lesions showed significantly higher RI as compared to the benign lesions,¹ vascular resistance index more than or equal to 0.69 is found to be 84.2% sensitive and 88.9% specific for the detection of the malignant breast nodules. The advantage of RI is that it is used in situations where angle correction and velocity estimation are not possible.¹ It reflects the degree of the distal resistance.¹ Colour Doppler vascularity changes in breast cancer correlates with the histological response.⁹ Study conducted by David E Ibikunle in a five year review conducted from 1st January 2010 to 31st December 2014 in Nigeria showed that sensitivity of FNAC of breast lump keeping histopathology as gold standard in determining the final histologic diagnosis was found to be 99.4%, specificity of 100% and diagnostic accuracy of 86.3%.¹⁰

The validation of the study is to confirm the value of resistance index measured through the colour Doppler ultrasound as more than or identical to 0.69 for the recognition of the malignant breast lesions before biopsy and histopathology. This value of vascular resistance index is selected as less previous research work has been done on it. Prompt diagnosis will lead to instant decision making for the timely management of breast cancer.

Methodology

The study was conducted by the department of Radiology at Quaid-e-Azam international hospital from 11th February 2021 to 10th August 2021. After

approval from institutional ethical review committee. Sample size was calculated by using sensitivity specificity calculator taking Prevalence of Breast Ca = 38%,² Sensitivity of RI = 84.2%,¹ Specificity of RI = 88.9%,¹ Margin of error = 10% and Confidence level = 95 %. Total 215 patients with mean age of 47.79 – 6.64 years (31-50 years) were recruited from OPD and wards of the surgical units of Quaid-e-Azam international hospital, Islamabad fulfilling the inclusion criteria were selected by non-probability, consecutive sampling. Informed consent was taken from the patients for inclusion in the study and for the procedure after explaining the pros and cons. History regarding the breast cancer was taken. Examination was done to see breast lumps, to see inflammatory of the infective changes in the breast.

In all the patients breast lumps were examined by ultrasonography on Grey scale with linear probe of 7.5MHz. then with the same probe Doppler ultrasound of the lesion was performed using either colour or power Doppler. Increased vascularity of the lesion was recorded and the resistance index of the vessels were calculated. Data was acquired and reported on Doppler sonographic work station and reviewed by consultant having more than 5 years of experience. All lesions visible on the grey scale were biopsied. Then aspirate was sent to the histopathologist. The histopathological report was taken from the laboratory with the patients permission as already mentioned. The information of Doppler ultrasound and histopathology regarding breast carcinoma is analyzed and is entered in the proforma.

Inclusion Criteria

1. Women age of 20-70 years with breast lump diagnosed clinically by the primary care physician or noted by the patient herself.
2. Irregular shaped, hard, fixed breast lump on palpation with/without palpable axillary lymph nodes.

Exclusion Criteria

1. Patients already gone through breast surgery, chemotherapy or radiotherapy (post-chemotherapeutic/radiotherapeutic changes were evaluated).
2. Patients with known connective tissue disorders as scleroderma.

3. Patients with diagnosed skin inflammation or infection of breast other than suspected for inflammatory breast ca.
4. Breast lumps developed during pregnancy and lactation.

Collected data was analyzed through computer software SPSS 25.0. Age was presented as mean and standard deviation. 2x2 contingency table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value and for resistance index taking histopathology as gold standard.

Results

A total of 215 patients were included in this study during the study period of six months from 11-02-2021 to 10-08-2022. Regarding age distribution, majority of the patients were between 31-50 years of age and minimum patients were < 30 years old. Mean age of the patients was 47.79 – 6.64 years (Tab.1). Breast cancer was positive on Resistive Index in 174 patients while 196 patients were positive on histopathology. 170 patients were true positive, 4 patients were false positive, 26 patients were false negative and 15 patients were true negative (Tab.2). Sensitivity, specificity and diagnostic accuracy of Resistive Index was 86.7%, 78.9% and 86.0%, respectively. Positive

Age (Year)	Number	Percentage
≤ 30	06	2.8
31-50	132	61.4
≥ 51	77	35.8
Total	215	100.0
Mean±SD	47.79 ± 6.64	

Table 1: Distribution of cases by age

Resistive Index	Histopathology (Gold Standard)		Total
	Positive	Negative	
Positive	170 (TP)	4 (FP)	174
Negative	26 (FN)	15 (TN)	41
Total	196	19	215

Sensitivity: 86.7%, Specificity: 78.9%, Positive Predictive Value (PPV): 96.7%, Negative Predictive Value (NPV): 36.6% and Diagnostic Accuracy: 86.0%

Table 2: Comparison of Resistive Index findings vs histopathology (n = 215)

predictive value and negative predictive value of Resistive Index was 97.7% and 36.6%, respectively.

Discussion

Ultrasonography is currently used as main tool to help mammography in the screening for malignant breast nodules.¹¹ Indications to mammography include the evaluation of lesions visible at mammography, palpable nodules without mammographic expression, as an assistance in the diagnosis of focal asymmetries, and patient with dense breast parenchyma to look for occult lesions. The main role of radiologist in management of patients with breast lumps is to accurately differentiate benign from malignant cases that will lead to early identification of the malignant cases having paramount importance in favorable prognosis and management of disease and avoid unnecessary invasive procedures such as core biopsy and fine needle aspiration in completely benign lesions. Doppler ultrasonography is a fast, cheap, and noninvasive method to evaluate vascularization, lots of studies have the efficiency of this method in discriminating between benign and malignant lesions.

Ultrasonography plays a significant role in the breast imaging evaluation. Color Doppler is used for assessing the vascularity of breast masses on ultrasound, to aid in determining the likelihood of malignancy. Thus, both the color Doppler signal generated in the underlying vasculature and its spectral wave form analysis have provided better determination of blood flow and characterization of vascularity pattern of underlying breast tissue.¹²

In study conducted by Ishrat Parveen at radiology department of CMH Multan from December 2015 to May 2016 had showed that diagnostic accuracy of RI in breast lesion examined by doppler ultrasound having specificity of 88.77%, positive predictive value (PPV) of 90.12%, negative predictive value (NPV) of 91.30% while diagnostic accuracy was calculated as 90.67%.¹³

In a study conducted by Mehrisirous between February 2010 and April 2013 with women referred to the sonography unit of two main hospitals of Isfahan, evaluated the role of doppler ultrasound in characterization of breast masses and concluded that resistive index (RI) value showed sensitivity of 75%

and high specificity of 97% for diagnosing breast carcinoma at a threshold value of 0.83.¹⁴

Choi et al. have speculated that the RI more than 0.70 in approximately 80% of malignant nodules having 80.9% sensitivity and 89.1% specificity.¹² Similar observation was done by Peters-Engl et al¹³ who have concluded that RI of 0.70 can be used as the best cut-off value for identification of malignant nodules having 81% specificity, 82% sensitivity, 89% negative predictive value and 70% positive predictive value.¹⁴ The results are similar to our study for breast malignancy identification having 86.7% sensitivity, 86.0% diagnostic accuracy, positive predictive value 97.7% and negative predictive value 36.6% with 78.9% specificity, for a RI cut-off value > 0.69. Similar observation was previously made as well by studies conducted by Peters-Engl C and Tariq M.^{15,16}

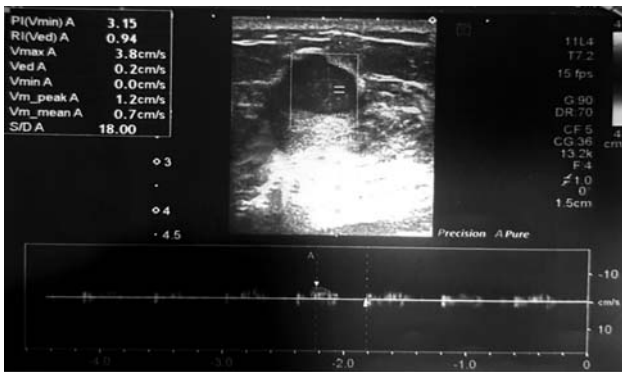


Figure 1: 60 years old female patient with well defined hypoechoic lesion having lobulated margins at 6 to 7 o clock position in lower inner quadrant of right breast parenchyma demonstrating RI of 0.95 on doppler images. Histopathology report showed it to be invasive ductal carcinoma.

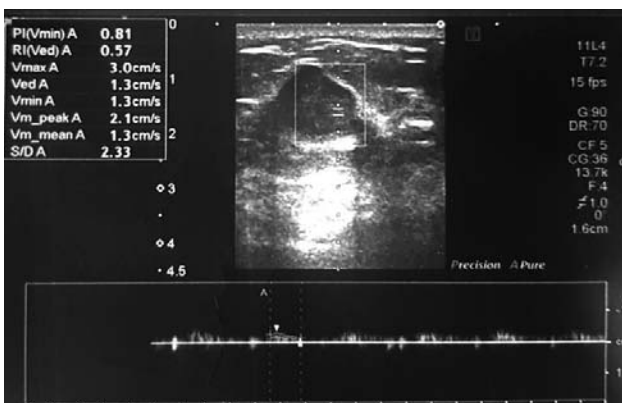


Figure 2: 30 years old female patient with well-defined hypoechoic lesion having lateral edge shadowing margins at 10 o clock position in upper inner quadrant of left breast parenchyma demonstrating RI of 0.57 on doppler images. Histopathology report showed it to be fibroadenoma.

Yang et al¹⁷ reported 98.4% sensitivity, 67.8% specificity, 38% PPV, 99.5% NPV, and 72.9% accuracy. In their study, the PPV was considerably lower, probably in relation to the different prevalence of breast cancer and to the different patient selection criteria.

Conclusion

This study proves diagnostic accuracy of resistance index measured through colour Doppler ultrasound of the breast lumps for diagnosing breast cancer in patients avoiding the need for biopsy. The results of the present study determine that a RI > 0.69 in a nodule > 1 cm suggests increased risk of malignancy, however additional information needs to be taken into consideration for selection of lesions eligible for histopathological study.

Conflict of Interest: None

References

1. Khan NH, Duan SF, Wu DD, Ji XY. Better reporting and awareness campaigns needed for breast cancer in Pakistani women. *Cancer Management and Research*. 2021 Mar 2;2:2125-9.
2. Fitzmaurice C, Allen C, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study [published correction appears in *JAMA Oncol*. Mar 2017; **3(3)**: 418]. *JAMA Oncol*. 2017; **3(4)**: 524-48.
3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*. Nov 2018; **68(6)**: 394-424.
4. Sohail, Saba, and Shams Nadeem Alam. "Breast

- cancer in Pakistan-awareness and early detection." (2007): 711.
5. Ward ZJ, Yeh JM, Bhakta N, Frazier AL, Atun R. Estimating the total incidence of global childhood cancer: a simulation-based analysis. *The Lancet Oncology*. Apr 2019; **20(4)**: 483-93.
 6. Begum N. Breast cancer in Pakistan: a looming epidemic. *J Coll Physicians Surg Pak*. Feb 2018; **28(2)**: 87.
 7. Monirujjaman Khan M, Islam S, Sarkar S, Ayaz FI, Kabir MM, Tazin T, Albraikan AA, Almalki FA. Machine learning based comparative analysis for breast cancer prediction. *Journal of Healthcare Engineering*. Apr 2022; 2022.
 8. Fatima S, Waheed S, Khan MI. Diagnostic accuracy of MR mammography in diagnosing malignant breast lesions taking histopathology as gold standard. *Journal of the College of Physicians and Surgeons Pakistan*. Jan 2019; **29(1)**: 16-8.
 9. Park AY, Seo BK, Han MR. Breast ultrasound microvascular imaging and radiogenomics. *Korean journal of radiology*. May 2021; **22(5)**: 677.
 10. Ibikunle DE, Omotayo JA, Ariyibi OO. Fine needle aspiration cytology of breast lumps with histopathologic correlation in Owo, Ondo State, Nigeria: a five-year review. *Ghana medical journal*. Apr 2017; **51(1)**: 1-5.
 11. Health Quality Ontario. Ultrasound as an adjunct to mammography for breast cancer screening: a health technology assessment. *Ontario health technology assessment series*. 2016; **16(15)**: 1.
 12. Moustafa AF, Cary TW, Sultan LR, Schultz SM, Conant EF, Venkatesh SS, Sehgal CM. Color doppler ultrasound improves machine learning diagnosis of breast cancer. *Diagnostics*. Aug 2020; **10(9)**: 631.
 13. Parveen I, Javed K, Elahi B, Nasrullah F, Mahmood R, Aamir MO. Evaluation of breast lesions with Doppler ultrasound: Diagnostic accuracy of resistive index as a predictor of malignancy. *The Professional Medical Journal*. Apr 2020; **27(04)**: 825-30.
 14. Choi HY, Kim HY, Baek SY, Kang BC, Lee SW. Significance of resistive index in color Doppler ultrasonogram: differentiation between benign and malignant breast masses. *Clinical imaging*. Sep 1999; **23(5)**: 284-8.
 15. Peters-Engl C, Medl M, Leodolter S. The use of colour-coded and spectral Doppler ultrasound in the differentiation of benign and malignant breast lesions. *British journal of cancer*. Jan 1995; **71(1)**: 137-9.
 16. Tariq M, Masood M, Khan TQ, Ahmad KK. Doppler sonography in the diagnosis of breast masses. *PJR* 2010; **20**: 80-3.
 17. Yang WT, Chang J, Metreweli C. Patients with breast cancer: differences in color Doppler flow and gray-scale US features of benign and malignant axillary lymph nodes. *Radiology*. May 2000; **215(2)**: 568-73.