

Diagnostic Accuracy of Contrast-Enhanced MRI for Detecting the Malignant Breast Lesions

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Author's Contribution

¹ Conception of study

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Article Processing

Received: 14/02/2020

Accepted: 22/02/2021

Cite this Article: Parveen, N., Butt, R.W., Niazi, M., Iqbal, K., Manzoor, S., Abid, A. Diagnostic Accuracy of Contrast-Enhanced MRI for Detecting the Malignant Breast Lesions. *Journal of Rawalpindi Medical College*. 30 Mar. 2021; 25(1): 26-30.

DOI: <https://doi.org/10.37939/jrmc.v25i1.1340>

Conflict of Interest: Nil

Funding Source: Nil

Access Online:



Abstract

Objectives: To determine the accuracy of contrast-enhanced MRI in the diagnosis and detection of breast lesions and their malignant potential by taking the gold standard of histopathology.

Materials and Methods: This study was conducted at the Department of Diagnostic Radiology, Pakistan Institute of Medical Sciences (P.I.M.S.) Islamabad. It was undertaken in collaboration with the Department of General Surgery P.I.M.S, Department of Pathology P.I.M.S Islamabad, and HIT Hospital Taxila. The study design was a cross-sectional (Validation) study and the duration of the study was 6 months (from 01-Oct-2016 to 31-Mar-2017).

Results: Sample size was calculated by using sensitivity and specificity calculator taking sensitivity 94%¹ with a precision of 6%, specificity 85%¹ with a precision of 10%, prevalence is 45.9%², and confidence interval of 95% it comes out to be 92%. Sample collection was made by the technique of Consecutive non-probability sampling.

Conclusion: Breast MRI imaging is a modern evolving modality. A gradual increase in diagnostic specificity is achieved with improved software and techniques. More such studies would help develop confidence in this advanced imaging modality for improving patient management and avoiding unnecessary biopsies.

Keywords: Diagnostic accuracy, MRI, histopathology, breast cancer.

Introduction

Breast cancer is the most common cancer in women being the second leading cause of death in women living in the developed world.¹ The average 5 years survival rate from breast cancer is 57% in the developing countries and 73% in the developed countries.

Around a million fresh cases of breast cancer are yearly diagnosed globally. It is the most commonly diagnosed cancer in females with a frequency of one in nine in the Pakistani population. This occurrence is 2.5 times higher than Iran and India being direct neighbourhood countries. Report from Shaukat Khanum Memorial Cancer hospital and research centre shows that currently, the incidence of breast cancer is 45.9% among female patients and 21.5% among all.

The gold standard for screening breast cancer is Mammography providing the high two-dimensional resolution (2D). Due to its limitations, three-dimensional structure in a single plane (3D) can be achieved by sonomammography or dynamic contrast-enhanced (DCE)-MRI of the breast. Secondary imaging is mandatory whenever there is a suspicious lesion found on conventional mammography.

Sonomammography gives useful insight in detecting tissue composition and providing additional information on dense breasts and cystic mass lesions. MRI of the breast however is superior to both conventional and Sonomammography being able to image the entire breast in thin slices comprising the entire breast volume and measuring differences in contrast uptake providing information about the vascular nature of breast lesions. Malignant lesions generally have a more profound blood supply but neovascularity has poor and leaky formation hence contrast take-up is different from benign lesions. Radiologists can hence distinguish different contrast kinetics of malignant and benign lesions leading to better differential diagnosis.

The hallmark of MRI for breast imaging is enhancement pattern² with gadolinium contrast. So comparing with other imaging modalities like mammography MRI supplies both morphology and vascularity (kinetics) of the tumour, increasing its sensitivity in the detection of malignancy. Early uptake and early washout is a typical pattern of malignant lesions. Images are typically taken at 45 seconds of gadolinium injection and then every one to two minutes, completing by 4 minutes to observe a rapid enhancement of malignant breast lesions.

Breast magnetic resonance imaging (MRI) can be used as a screening tool in young women with high-risk factors for breast cancer. It has a determining role in the estimation of the local staging of cancer and response to neoadjuvant chemotherapy. MR Breast can also help in evaluating borderline lesions classified so by Core needle biopsy.³ For lesions having non-suspicious enhancement patterns or remaining unenhanced at breast MR imaging, follow-up scanning may be pursued instead of biopsy. Further advancements in DCE-MR imaging with higher-temporal-resolution and onerous quantitative analyses of the temporal enhancement curves⁴ are recently a research avenue.

This study aims to discuss potential uses of contrast-enhanced MRI of the breast, in detecting malignant breast lesions as they are the most frequently diagnosed cancers among Pakistani females. It is a non-invasive imaging modality with no ionizing radiation. As it is not routinely used as a primary diagnostic modality here in Pakistan its diagnostic accuracy in detection of malignant and benign breast lesions requires to be established to prove or disprove its superiority in comparison with mammography and ultrasound. There will be an increased public awareness regarding this common and manageable disease.^{5,6}

Materials and Methods

After taking approval from the institutional review board and ethics committee, this study was conducted at the Department of Diagnostic Radiology, Pakistan Institute of Medical Sciences (P.I.M.S.) Islamabad. It was undertaken in collaboration with the Department of General Surgery P.I.M.S, Department of Pathology P.I.M.S Islamabad, and HIT Hospital Taxila. The study design was a cross-sectional (Validation) study and the duration of the study was 6 months (from 01-Oct-2016 to 31-Mar-2017). By using sensitivity and specificity calculator taking sensitivity 94%(1) with a precision of 6%, specificity 85%(1) with a precision of 10%, prevalence is 45.9%(2), and confidence interval of 95% a minimum of 92 patients were required as the sample size. The sampling Technique was Consecutive non-probability sampling.

During the study period female patients aged 20 to 60 years who had the suspicion of breast cancer based on clinical examination (having palpable lump with irregular margins, fixed to the chest wall, and associated skin edema.), Ultrasound features (taller than wider hypoechoic lesion with irregular margins,

increased vascularity on color Doppler). And/ or Mammographic abnormality (hyperdense lesion with speculated margins, architectural distortion, microcalcifications, associated skin thickening) were included. Those excluded were patients with known breast malignancy on biopsy, with recent breast surgery and radiotherapy (within 6 months of MRI.), with recurrence of the disease, and Claustrophobic patients unable to undergo MR scanning.

After obtaining written and informed consent, patients were booked for dynamic contrast-enhanced MR imaging of both breasts on a 1.5-tesla magnet by using a dedicated bilateral breast surface coil. The procedure and protocol of the examination were explained to the patient and it was declared clearly that it is a research study. Demographic features were recorded on the Performa by me. An ethical code of conduct was maintained and a female chaperone or doctor was present for female patients at the time of imaging. The scans were viewed by a single consultant radiologist at P.I.M.S. diagnostic radiology department. The patient's course of management was meticulously followed by the trainee researcher till the biopsy is performed and sent to departments of pathology for histopathology. Histopathological diagnosis was then be correlated with the findings of the contrast-enhanced MRI breast.

The data were analyzed in SPSS version 10. A 2 x 2 table was used to determine sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic efficacy. Mean for numerical data like age and frequency percentages for categorical data like a true positive, true negative, false positive, and false negative was calculated.

Results

An aggregate of 92 patients was analysed for determining the accuracy of contrast-enhanced MRI as a diagnostic tool in detecting malignant breast lesions by taking the gold standard of histopathology. The results were analysed as follows:

Age variation among 92 analysed patients was as, 31(34%) patients in the age range 31-40 years, 44(48%) patients in the age range 41-50 years, 17(18%) patients in the age range 51-60 years. The mean age of subjects was 42 years, SD being ± 2.16 . (Table 1)

Histopathology findings among 92 patients were analysed as 89(97%) patients had malignant lesions while 3(3%) patients didn't have malignant lesions (Table 2)

MRI findings among 92 patients were analysed as 83(90%) patients had malignant lesions while 9(10%) patients didn't have malignant lesions (Table 3)

Accuracy of diagnosis of MRI with Histopathology taken as the gold standard was analyzed. MRI had a sensitivity of 92%, Specificity of 67%, Positive predictive value (PPV) of 99%, Negative predictive value (NPV) of 22%, and Diagnostic accuracy of 91%. (Table 4)

Table 1: Age Distribution (n=92)

| Age | Frequency | Percentage |
|-------------|-----------|------------|
| 31-40 years | 31 | 34% |
| 41-50 years | 44 | 48% |
| 51-60 years | 17 | 18% |
| Total | 92 | 100% |

Mean age was 42 years with SD ± 2.16

Table 2: Malignant Lesions on Histopathology (n=92)

| Histopathology | Frequency | Percentage |
|----------------|-----------|------------|
| Present | 89 | 97% |
| Absent | 3 | 3% |
| Total | 92 | 100% |

Table 3: Malignant Lesions on MRI (n=92)

| MRI | Frequency | Percentage |
|---------|-----------|------------|
| Present | 83 | 90% |
| Absent | 9 | 10% |
| Total | 92 | 100% |

Table 4: MRI vs. Histopathology Findings (n=92)

| | | Histopathology | | |
|-------|----------|----------------|---------------|----------|
| | | Positive | Negative | Total |
| MRI | Positive | A82(99%) TP | B1(1%) FN | 83(90%) |
| | Negative | C7(78%) FP | D2(22%) TN | 9(10%) |
| Total | | 89(97%) | 3(3%) | 92(100%) |

Sensitivity = $82/82+7*100 = 82/89*100 = 92\%$

Specificity = $2/2+1*100 = 2/3*100 = 67\%$

Positive predictive value = $82/82+1*100 = 82/83*100 = 99\%$

Negative predictive value = $2/7+2*100 = 2/9*100 = 22\%$

Diagnostic Accuracy = $82+2/92 *100 = 84/92*100 = 91\%$

Discussion

Breast cancer is the most common cancer in women being the second leading cause of death in women living in the developed world. Around a million fresh cases of breast cancer are yearly diagnosed globally. It

is the most commonly diagnosed cancer in females with a frequency of one in nine in the Pakistani population. This occurrence is 2.5 times higher than Iran and India being direct neighborhood countries. Report from Shaukat Khanum Memorial Cancer hospital and research center shows that currently, the incidence of breast cancer is 45.9% among female patients and 21.5% among all. Approximately 10 fold variation is seen among different countries of the world in incidence of breast cancer.

Malta and Cyprus have the highest age-related mortality (29.6 per 100,000 population) for breast cancer, while Haiti has the lowest mortality (2.0 per 100,000 population).⁷ Generally the incidence rates are higher in Europe and lower in Africa and Asia.⁸ The commonest cancer in women in the UK remains Breast cancer and it accounts for 31% of the reported cases.⁹ Impending risk for the immigrant women from low to high-risk countries also shows an ascending trend depicting a relation with environmental factors, lifestyle¹⁰ and dietary and drug habits.

In the last decade of the twentieth century, the use of hormone replacement therapy (HRT) was increase and is proposed to have a contribution to increasing incidences of breast cancer.¹¹ Under the age of 50 and premenopausal women at the time of diagnosis of breast cancer are less likely to having ER/ PR-positive lesions. On contrary, postmenopausal and older females usually have breast cancers responding to hormonal therapy. The consolidated magnitude of propensity from chemotherapy is less than that seen in premenopausal or younger women.^{12,13} The Aromatase Inhibitors (AIs) are evaded customarily in younger females due to concerns regarding diminished feedback of oestrogen on the pituitary and hypothalamus leading to increased Gonadotropin secretion and ovarian stimulation, causing increased androgen substrate and aromatase.^{14,15,16}

In our study mean age was 42 years with SD \pm 2.16 with 34% patients in the age range 31-40 years, 48% patients in the age range 41-50 years, and 18% patients in the age range 51-60 years. According to histopathology findings, 97% of patients had malignant lesions while 3% of patients didn't have malignant lesions. According to MRI findings, 90% of patients had malignant lesions while 10% of patients didn't have malignant lesions. Accuracy of breast MRI in diagnosis with the gold standard of Histopathology show MRI having a sensitivity of 92%, Specificity of 67%, Positive predictive value (PPV) of 99%, Negative predictive value (NPV) of 22%, and Diagnostic accuracy of 91.

A study conducted at The Johns Hopkins University further made use of kinetic curve type assessment in conjunction with high-resolution 3D breast MRI offering improvement in the diagnostic performance of Diagnostic MRI.¹⁷

Diagnostic sensitivity of breast MR in detecting breast cancer is high approaching almost 100% for invasive malignant lesions. Nevertheless, the specificity varies between 37-70% and hence is comparatively low.¹⁸ Factors leading to this wide range of specificity depend on differences in the study population, machine sophistication, applied protocols, and criteria for interpretation. Several studies conducted in the past should be consulted for improving the specificity.¹⁹

In a study conducted by Siegman et al²⁰, it was demonstrated that both qualitative and quantitative lesion characteristics were required for diagnostic identification of the lesion. Another study conducted by Khatri et al²¹ it was shown that better specificity could be gained by quantifying the pattern of enhancement. This method however utilised complex analysis involving mathematical formulations. We demonstrated in our study that the physical appearance of the lesion, post-contrast enhancement, and qualitative assessment of time signal intensity curves are pertinent imaging parameters for MRI evaluation in increasing diagnostic confidence. Our results are hence consistent with major previous studies.^{22,23} MR imaging is in progressing phase in most clinical setups in Pakistan. Our results are relatable to many previous studies but still, we have several limitations. This is because of the cost factor and lack of awareness regarding the usefulness of MR imaging for the diagnosis of breast cancer. It is needed that more such studies are carried out in the Pakistani population to get a database for our ethnic and environmental factors.

Conclusion

Our study concludes that MRI breast is an emergent diagnostic modality. The major drawback of this non-invasive tool was its decreased specificity for malignant breast lesions. Various studies have nevertheless demonstrated that with better equipment and refined techniques the specificity shows a gradual increase. Further similar studies are required for establishing affirmation. This developing diagnostic tool if carefully utilized can help in for improved management of patients and reduce the load of unneeded biopsies.

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