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Original Research Article

Role of magnetic resonance imaging in detection of metastatic axillary lymph nodes in breast cancer patients

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ABSTRACT

Background: Magnetic resonance imaging has been evolved as a very important tool in diagnosing the axillary lymph nodes pre-operatively. In recent studies, in women with various risk profiles, the sensitivity ranges between 81% and 100%, which is approximately twice as high as the sensitivity of mammography.
Methods: This prospective study was performed at PGIMS, Haryana from December 2018 to March 2020. Total 30 patients (n=30) were included in the study. All the patients presenting with clinically palpable breast lump, underwent triple assessment test. All the patient underwent modified radical mastectomy and the final histopathological report of the specimen was then compared with the preoperative clinical and MRI assessment of the metastatic axillary lymph nodes.
Results: This study aimed at detection of axillary lymph node metastasis in breast malignancies by breast MRI. The sensitivity of this MRI came to be about 80.00%, specificity of about 80%, positive predictive value of about 95.24%, negative predictive value of about 44.44% and accuracy of about 80.0% with 95% confidence interval.
Conclusions: Magnetic resonance imaging is a very important investigation in detection of breast malignancies, their depth, muscles and skin involvement as well as axillary lymph node detection. Axillary lymph nodes can although be detected by clinical examination, but problem lies in their sensitivity and specificity as axillary lymph nodes of small size cannot be detected by clinical examination.

Keywords: Breast cancer, Breast malignancy, MRI, Axillary lymph nodes, Metastatic axillary lymph nodes

INTRODUCTION

Magnetic resonance imaging (MRI) has been evolved as a very important tool in diagnosing the axillary lymph nodes (ALN) pre-operatively. Multiple studies in the first decade of the 21st century have established contrast-enhanced breast MRI as a screening modality for women with a hereditary or familial increased risk for the development of breast cancer. In recent studies, in women with various risk profiles, the sensitivity ranges between 81% and 100%, which is approximately twice as high as the sensitivity of mammography. The specificity increases in follow-up rounds to around 97%, with positive predictive values for biopsy in the same range as for mammography.[1] Without complete staging information, physicians must rely on surrogate markers indicating the risk for high axillary disease and thereby choose appropriate targeted therapy.[2] The development of magnetic resonance imaging (MRI) for use in medical investigation has provided a huge forward leap in the field of diagnosis, particularly with avoidance of exposure to potentially dangerous ionizing radiation. With decreasing costs and better availability, the use of MRI is becoming ever more pervasive throughout clinical practice.[3] The sensitivity of breast MRI is reported to be very high (over 90%) but the specificity is still low to moderate (72%) making the discrimination between benign and malignant lesions challenging. Since 2000,

breast MRI has been extensively used and has become an important modality in high-risk screening, diagnosis, staging and follow up of breast cancer. Breast MRI provides the best imaging correlation with pathology and many studies have shown the MRI is superior to clinical assessment, mammogram and ultrasound.[4-6]

Aim and objectives

The main objective of the study was to do MRI in breast cancer patients undergoing MRM to study axillary lymph node status, to study histopathological report of specimen of MRM and to correlate the result of MRI with that of histopathological findings of lymph nodal metastasis to assess the role of MRI in detection of axillary lymph nodes in breast cancer patients.

METHODS

After approval of the ethical justification committee, this prospective study was performed in PGIMS, Haryana from December 2018 to March 2020. Total 30 patients (n=30) were included in the study. All the patients presenting with clinically palpable breast lump, underwent triple assessment including clinical examination, radiological assessment and histopathological study by either fine needle aspiration cytology (FNAC) or core needle biopsy (CNB). All the patient whose biopsy came to be positive for malignancy underwent additional magnetic resonance imaging in whom axillary lymph node was not palpable.

Inclusion criteria

Inclusion criteria for current study were; patients to be operated for MRM and FNAC/biopsy proven malignant breast lump.

Exclusion criteria

Exclusion criteria for current study were; benign breast lump and patients not requiring surgery i.e. stage 4 breast cancer.

Procedure

In comparison with previously researches that have been performed, study is being done to assess MRI in 30 breast cancer patients undergoing MRM to study axillary lymph node status correlating with histopathological report of specimen of MRM. The sensitivity found in articles ranges 50% to 80%. Therefore, assuming (p)=70% as the sensitivity with 10% margin of error, the minimum required sample size at 5% level of significance is 81 patients the sample size was calculated using the formula:

$$n = \frac{Z^2_{\alpha/2}\, pq}{d^2}$$

where p is the observed sensitivity of breast cancer patients undergoing MRM to study axillary lymph node status, q=1–p, d is the margin of error, $Z_{\alpha/2}$ is the ordinate of standard normal distribution at α% level of significance. Since the study is time bound, all consecutive patients meeting the convenient eligibility criteria during the study period will be enrolled. It is expected from the previous experience that about 30 patients will be enrolled.

Statistical analysis

Statistical testing will be conducted with the statistical package for the social science system version SPSS 20.0. Continuous variables will be presented as mean SD or median (IQR) for non-normally distributed data. Categorical variables will be expressed as frequencies and percentages. Nominal categorical data between the groups will be compared using Chi-square test or Fisher's exact test as appropriate. The area under the curve, the sensitivity, and the specificity will also be calculated to analyse the diagnostic accuracy of MRI in breast cancer patients undergoing MRM to study axillary lymph node status correlating with histopathological report of biopsy specimen of MRM. For all statistical tests, a p value less than 0.05 will be taken to indicate a significant difference.

Axillary lymph nodes were determined to be malignant according to their size, cortical thickness, long axis to short axis ratio, the presence of a fatty hilum and contrast enhancing patterns whether homogenous or heterogenous was also accredited. The different sequences involved while doing the MRI has been depicted in table 1 while the best sequence for detection of MALN in breast carcinoma was T2 FSE ASPIR (fast spin ECHO). Both the patients of early breast cancer (EBC) and locally advanced breast cancer (LABC) in whom axillary lymph node was not palpable after receiving neo-adjuvant chemotherapy were included in the study to assess the non-palpable metastatic axillary lymph nodes. All the patient underwent modified radical mastectomy up till level 3 axillary lymph node dissection (ALND). The final histopathological report of the specimen was then compared with the preoperative clinical and MRI assessment of the metastatic axillary lymph nodes. The diagnostic accuracy of MRI was then compared to the final tissue reporting for axillary lymph nodes.

RESULTS

Based on the TNM classification of Breast cancer, it is divided in two categories i.e. early breast cancer and locally advanced breast cancer. In this study majority of the patients were EBC malignancies comprising 60% and the rest were LABC comprising of 40%. Magnetic resonance imaging is a very useful investigation in detection of metastatic axillary lymph nodes (MALN) in

breast carcinoma. In this study, comparison of MRI with EBC/LABC has been shown in (Table 2) and comparison of EBC/LABC with HPR has been shown in (Table 3).

Table 1: Sequences involved in the MRI breast.

Sequence	TE (msec) (time of ECHO)	TR (msec) (time of repetition)	Slice thickness (mm)	Slice gap (mm)	Fat suppression	Phase FOV (cm) (field of view)	NEX (number of excitation)
T2 FSE ASPIR (fast spin ECHO)	102	8652	4	1	Yes	35	2
T2 FSE	102	5983	4	1	No	35	2
T1	MIN full (8.4)	3000	4	1	No	35	1
TIFS (T1 fat suppression)	MIN full (8.4)	3000	4	1	Yes	35	1
DWI STIR	MIN (61.9)	4896.1	4	1	No	35	2
DX vibrant (dynamic scan)	2.1	5.3	2	0	Yes	-	-
SAG T2 FS	102	8935	4	1	Yes	20	2

Table 2: Comparison of MRI with EBC/LABC with p value=0.13.

MRI vs. EBC/LABC			EBC/LABC		Total
			EBC	LABC	
MRI showing MALN	**No**	**N**	2	4	6
		%	11.1%	33.3%	20%
	Yes	**N**	16	8	24
		%	88.9%	66.7%	80%
Total		**N**	18	12	30
		%	100%	100%	100%

Table 3: Comparison of EBC/LABC with HPR with p value=0.25.

HPR vs. EBC/LABC			EBC/LABC		Total
			EBC	LABC	
HPR showing MALN	**No**	**N**	4	5	9
		%	22.2%	41.7%	30%
	Yes	**N**	14	7	21
		%	77.8%	58.3%	70%
Total		**N**	18	12	30
		%	100%	40%	100%

MRI images showing tumor involving breast tissue with malignant axillary lymph nodes has been depicted in (Figure 1) while the histopathological images of both normal and metastatic lymph node that has been dissected out were depicted in (Figure 2). Comparison of MRI for detection of MALN pre-operatively with MALN as shown by HPR for the same in breast cancer patients has been shown in (Table 4 and Figure 3). This study aimed at detection of axillary lymph node metastasis in breast malignancies by breast MRI. Diagnostic accuracy of magnetic resonance imaging in detection of axillary lymph node metastasis with its different efficacy of this study has been shown in (Table 5).

Table 4: Comparison of MRI with HPR for diagnostic accuracy for detection of malignant axillary lymph nodes in breast cancer patient with p value=0.01.

MALN detection in MRI as compared to HPR			MRI showing MALN		Total
			No	Yes	
HPR showing MALN	**No**	**N**	5	4	9
		%	83.3%	16.7%	30%
	Yes	**N**	1	20	21
		%	16.7%	83.3%	70%
Total		**N**	6	24	30
		%	100%	100%	100%

DISCUSSION

The principle aim of the study was to assess whether MRI is an important investigation in identifying the metastatic axillary lymph nodes. So in this study we systematically reviewed the current literature on diagnostic performance of MRI on detection of metastatic axillary lymph nodes in breast cancer patients. Different methods have been implicated in identifying the metastatic axillary lymph nodes pre operatively in breast cancer patients such as mammography, ultrasound, computed tomography and magnetic resonance imaging. We sought to correlate the use of magnetic resonance imaging for detection of

axillary lymph node metastasis pre operatively as compared to that shown on the histopathology reports.[7-10]

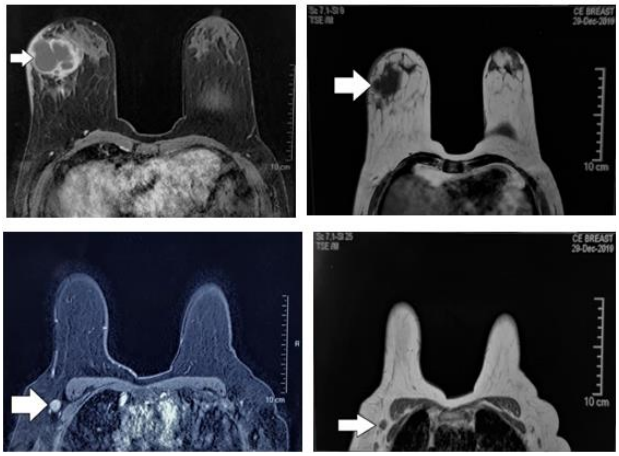

Figure 1: MRI showing malignant breast tumor (LABC) in right breast (both upper images) and MALN in right axilla (both lower images).

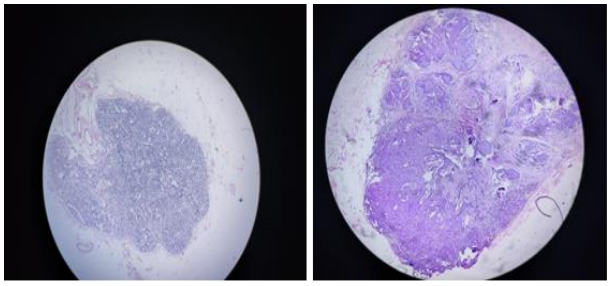

Figure 2: Histopathology report showing non-malignant (left image) and malignant (right image) axillary lymph nodes.

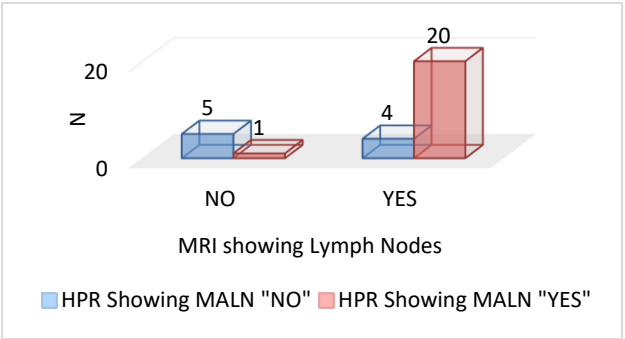

Figure 3: Histogram showing comparison of HPR with that of MRI for detection of MALN.

Axillary lymph node metastasis is one of the main factors affecting the prognosis of patients with breast cancer, and the 5-year survival for breast cancer patients has been changed according to the nodal affection; for example, in node-negative disease it measures 82.8% compared with 73% in 1-3 positive nodes, 45.7% in 4-12 positive nodes, and 28.4% in cases with more than 13 positive nodes.[11-13] However, diagnosis of these nodes currently requires pathologic analysis of the tissue biopsy or dissection after surgery which is considered the gold standard for diagnosis; unfortunately both of them are invasive procedures.[14] The investigators made extensive effort to develop a non-invasive technique that accurately preoperatively assesses both sentinel and distant axillary lymph nodes metastasis, aiming to reduce the time and the cost of diagnosis as well as the risk of complication to the patients due to unnecessary axillary sampling.[15] Breast carcinoma is classified according to the TNM (tumour, node and metastasis) classification which is further staged. Based on staging, breast carcinoma can be divided into EBC and LABC. In the current study, 60% of the population were early breast cancer while the rest 40% were locally advanced breast cancer. In the study done by Lee B et al, 75.89% of the patients presented as early breast cancer while the remaining presented as locally advanced breast cancer.

Table 5: Diagnostic accuracy of magnetic resonance imaging in detection of axillary lymph node metastasis.

Statistics	Value (%)	95% CI (%)
Sensitivity	80.00	59.30 to 93.17
Specificity	80.00	28.36 to 99.49
Positive predictive value	95.24	77.41 to 99.15
Negative predictive value	44.44	24.58 to 66.26
Accuracy	80.00	61.43 to 92.29

In the current study, MRI showed 24 patients out of 30 patients with MALN pre operatively i.e. 80% in which 20 were true positive i.e. 83.3% MALN as shown by the histopathology report and 4 were false positive i.e. 16.7%. Six patients out of 30 patients were shown by MRI to be not having MALN in which 5 patients were true negative who actually do not have any MALN i.e. 83.3% as shown by the HPR and 1 patient out of 6 patient i.e. 16.7% was false negative that means they actually have positive MALN as shown by the HPR but MRI was not able to detect it. Comparison of MRI for detection of MALN pre-operatively with HPR for the same has been shown in (Table 4). The p value of the study came out to be 0.01.

Although the histopathology of tissue is still the gold standard diagnostic tool for breast malignancies. Other diagnostic tools such as magnetic resonance imaging can also be used for diagnosis. This current study has shown that MRI has higher sensitivity in detection of malignant axillary lymph nodes but less specificity as compared to other studies. This difference in sensitivity and specificity can be attributed to the small sample size of the current study (n=30). The bizarre value of negative predictive value is an incidental finding and can also be attributed to small sample size. The diagnostic performance and their values are as par comparable to other studies and is non-significant. With the result of NPV of 44% and specificity of 80% (very wide confidence interval) in this

study, it projects that we would need to biopsy/FNAC all axillary LN to confirm diagnosis. This can be attributed to the small sample size of n=30. As per the peer articles comparison, in which the sample size was large, NPV came out to be more than 80%. Hence FNAC is not required in cases where MRI is showing the ALN to be metastatic.

Table 6: Study comparison of diagnostic performance of MRI.

Study		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Schipper et al[9]	Node by node	55.00	93.00	60.00	91.00	---
	Patient by patient	67.00	87.00	62.00	89.00	---
Yoshimura et al[16]		79.00%	93.00	89.00	87.00	88.00
Zaiton et al[10]		94.50%	93.60	96.00	94.70	95.60
Arslan et al[7]		73.03%	95.00	91.67	82.61	85.71
Current study		80.00%	80.00	95.24	44.44	80.00

When the current study is compared with the existing peer articles, the results has remarkably shown that the MRI is a better investigation tool than the existing clinical examination, mammography, and ultrasound technique. A new trial has also come namely the SOUND trial (SOUND: Sentinel node vs. Observation after axillary UltraSouND), stating to abandon SLNB in EBC after USG showing ALN negative status.[17]

As per the recent technical advances in MRI, the availability has gone easy with reduction in cost of imaging. But till date, doing MRI requires expertise and a handsome amount of money for set-up. Although overall detection of metastatic ALN is better in MRI than USG, MRI guided FNAC/biopsy is expensive and technically difficult and cumbersome as compared to the USG guided FNAC which is an easier and much cheaper staging modality. Hence the only limitations of the MRI are availability, high cost and expertise for doing MRI-guided FNAC of axillary lymph nodes.

CONCLUSION

Breast carcinoma is a very common disease among women of reproductive age group. Hence its early diagnosis is very essential. Its accurate diagnostic methods are being evolved over time but very few of them hold the true status of malignancies. Magnetic resonance imaging is a very important investigation in detection of breast malignancies, their depth, muscles and skin involvement as well as axillary lymph node detection. Axillary lymph nodes can although be detected by clinical examination, but problem lies in their sensitivity and specificity as axillary lymph nodes of small size cannot be detected by clinical examination. Apart from the current guidelines for use of MRI in breast cancer patient, although surgery still remains the gold standard to stage the axillary lymph nodes in cases of breast cancer, MRI can also be used pre-operatively in breast cancer patients for the detection of axillary lymph node metastasis thereby reducing the need for cumbersome axillary lymph node dissection.

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