Original Article

Diagnostic Accuracy of Diffusion Weighted Magnetic Resonance Imaging (DW-MRI) for Skeletal Metastasis in Patients of Breast CA in Comparison with Bone Scan

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Abstract

Background: Breast carcinoma (CA) is one of the most prevalent cancers in women all across the globe. In current clinical practice, bone scan is main method for determining metastasis. However, use of various other imaging such as whole body magnetic resonance imaging (WB-MRI), enhanced with diffusion weighted protocol, can provide with a significant alternative method in early detection and assessment of various treatment options.

Objective: To evaluate diagnostic accuracy of diffusion weighted MRI (DW-MRI) for skeletal metastasis in patients of breast CA taking bone scan as a gold standard.

Methods: It was a cross sectional study, carried out at Department of Radiology, Mayo Hospital Lahore. 106 patients were enrolled and sent to the department of nuclear medicine for bone scan as part of their routine bone metastatic work-up. MRI including conventional sequences as well as DW sequence was then performed in all patients.

Results: Mean age of patients was 51.2±11.7 years. On bones scan, metastasis were identified in 86 (81.1%) patients, while it was negative in 20 (18.2 %) patients. On DWI, metastatic disease was found in 73 (68.8%) patients, while it was absent in 33(31.1%) patients. Sensitivity, specificity, PPV and NPV of DWI-MRI were 80.1%, 80.0%, 94.5% and 48.4%, respectively.

Conclusion: Sensitivity and specificity values of DWI are satisfactorily high in detecting metastatic disease in patients of breast CA. It can be a reliable and noninvasive alternate in detection of early disease.

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Introduction

Breast cancer (CA) is the most prevalent cancer in females and a predominant cause of death worldwide. More than 2 million new cases were diagnosed in 2020, and the incidence has been increasing each year.[1] These statistics are even worse in Pakistan, with a reported prevalence of 1 in every 9 women at some point in their lives.[2] According to a recent study, breast cancer accounted for 24.1% of all cancers in Pakistan.[3] As it is associated with high rates of morbidity and mortality, early detection and correct diagnosis are necessary for improved patient outcomes.[4] Almost 77%

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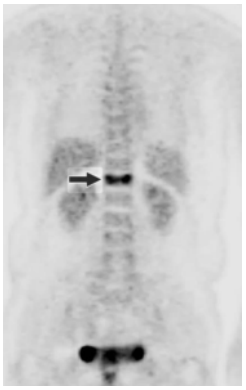
invasive CA cases arise in women over the age of 50, but with early diagnosis, survival rates can reach up to 90%.[4]

Skeletal metastasis is a predominant form of bone malignancy and is particularly found in advanced breast cancer, with an estimated occurrence of approximately 70%.[5] The treatment approach for breast cancer is highly influenced by the diagnosis of bone metastasis.[6] Therefore, detection of bone metastasis is crucial in staging and treatment planning of these patients. Conventional diagnostic methods for skeletal metastasis, such as bone scintigraphy (bone scan), have been widely used,[7,8] but recent advances in imaging technology, such as diffusion-weighted magnetic resonance imaging (DWMRI), also offer higher diagnostic accuracy.[8-10]

Bone scintigraphy, or bone scan, has long been considered a gold standard for detecting skeletal metastasis, with sensitivity and specificity rates of 83% and 96%, respectively.[11] It uses a radiotracer to highlight areas of increased bone turnover and is widely accessible and relatively inexpensive.[12] However, bone scans sometimes yield false positive or false-negative results, particularly in cases of early metastasis or when lesions are in sites with low metabolic activity.[13]

On the other hand, DW-MRI is a non-invasive technique, involving no radiation and contrast agent administration.[14] It measures the movement of water molecule within tissues. Recent studies have documented the promising results of DW-MRI in identifying skeletal metastasis,[14] but further research is necessary to establish its role in clinical practice. According to a study, the sensitivity of DW-MRI was 81.8% and its specificity was 86.4%.[15]

It is important to detect metastatic disease early to ensure appropriate and timely treatment. So, the rationale of this study was to find and compare the diagnostic accu-racy of bone scan and DW-MRI for metastasis in CA breast patients. Although many researches are being conducted internationally, data is lacking in our local settings, where the inci-dence is alarmingly high. This study would not only help in gathering substantial data in our population, but also help in strategizing new treat-ment plans suitable for the population in this part of the world.



Methods

It is a cross-sectional study, carried out at Department of Radiology, Mayo Hospital, Lahore, using 1.5 tesla, General electronics American machine, model Signa voyager in 6 months (Jan15, 2019-july 15 2019). A sample size of 106 is calculated at 95% confidence interval and taking expected frequency of breast cancer as 70% and sensitivity and specificity of DW MRI as 81.8% and 86.4% with 10% margin of error respectively.[15] Approval was taken from ethical committee (No. 361/RC/KEMU) and informed consent was taken from all patients.

One hundred six patients of age 22-70 years, presenting with pathological diagnosis of breast CA were selected by non-probability consecutive sampling. Patients with breast lump without biopsy proven breast CA, those with metallic implants making them contraindicated for MRI, claustrophobic patients not willing to undergo MRI, those with unstable cardiac, neurological or psychiatric disease assessed by history, physical examination, and clinical record, and those who were already undergoing chemotherapy or treated with chemotherapy within previous 03 months, those who are having documented bone infection previously were not included.

Demographic details were noted on a predesigned questionnaire. All patients were then sent to the department of nuclear medicine for bone scan as a part of their routine examination for bone metastatic disease. After that, Whole-body DW-MRI was performed along with other routine sequences using a spin-echo (SE) sequence with a short TE (35 ms) and a long TE (144 ms). Patients were labeled as positive or negative based on the results of the DW-MRI, where a positive result indicated the presence of skeletal metastasis and a negative result indicated no evidence of metastasis.

All the data was analyzed in SPSS version 21. Numerical variables such as age, and duration of disease were presented by mean and standard deviation. Data was then stratified for age, and duration of disease. Post stratification 2x2 table was generated to calculate the PPV, NPV, sensitivity, specificity and accuracy of DWI in comparison with bone scanning.

Results

A total of 106 patients were included in the study. Descriptive statistics of demographic variables are presented in table 1. Mean age of patients was 51.2 years with standard deviation of 11.7. Mean duration of disease was 6.2 ± 2.7 months. There were 21 females (19.8%) who were 22-40 years old, and 85 females (80.2%)

were 41-70 years old.

Diagnostic accuracy of DW-MRI for metastasis with bone scan as the gold standard is given in table 2. On DW-MRI, metastasis were found in 73 (68.8%) patients, while it was negative in 33 (31.1%) patients. On bone scan, metastasis were identified in 86 patients (81.1%) and negative in 20 patients (18.8%). Sensitivity and specificity of DW-MRI was 80.2% and 80% respectively.

When the data was stratified by age, the sensitivity and specificity for the 22-40 years age group were 70% and 100%, respectively. In contrast, for the 41-70 years age group, the sensitivity and specificity were 83% and 78.9%, respectively. On stratification of data according to the duration of the disease, the sensitivity and specificity for a duration of less than 6 months were 82.6% and 78.5%, respectively. In contrast, for a duration of more than 6 months, the sensitivity and specificity were 77.5% and 83%, respectively.

Table 1: *Descriptive statistics of age (years), BMI (kg/m²) and duration of disease (months)*

Variables		Mean ± standard deviation
Age (years)		51.2 ± 11.7
Age groups n (%)	22-40	21 (19.8%)
	41-70	85 (80.2%)
BMI (kg/m²)		23.4 ± 2.94
Duration of disease		6.2 ± 2.7

Table 1: n = number of patients; % = percentage of patients; kg/m² = kilogram per meter square

Discussion

Many advancements have been made in the treatment of early-stage breast cancer; however, in 20-30% of cases, patients experience relapse in the form of metastatic disease.[16] Gradually, there has been an improvement in the early detection of metastatic disease radiologically through various methods. An emerging imaging technique for assessing bone marrow metastasis is DW-MRI, which has several advantages over other methods.[17] However, there is lack of local data on this topic. So, this study was aimed to evaluate the diagnostic accuracy of Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) for detecting skeletal metastasis in breast cancer patients, using bone scintigraphy (bone scan) as the gold standard. The sensitivity and specificity of DW-MRI observed in this study were notable, where it exhibited a sensitivity of 80.1% and a specificity of 80%. A previous study compared bone scan with MRI and provided encouraging results. The sensitivity and

Table 2: *Diagnostic Accuracy of DW-MRI for Metastasis with Bone Scan as the Gold Standard*

		Bone Scan						
		metastasis		Total	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
		Positive	Negative					
DW-MRI metastasis	Positive	69	4	73	80.1	80	94.5	48.4
	Negative	17	16	33				
Total		86	20	106				

Table 2: ppv = positive predictive value; npv = negative predictive value; DW-MRI = diffusion weighted magnetic resonance imaging.

Table 3: *Diagnostic accuracy of DW-MRI for metastasis taking Bone scan as the gold standard with respect to age groups and duration of disease*

Age Groups (Years)	Skeletal metastasis on DW-MRI	Skeletal Metastasis on Bone scan		Sensitivity (%)	Specificity (%)	PPV(%)	NPV(%)
		Positive	Negative				
22-40	Positive	14	0	70	100	100	14
	Negative	6	1				
41-70	Positive	55	4	83	78.9	93	57
	Negative	11	15				
Duration of disease							
<3 months	Positive	38	3	82.6	78.5	92.6	57.8
	Negative	8	11				
3-6 months	Positive	31	1	77.5	83	96.8	35.7
	Negative	9	5				

Table 3: PPV = positive predictive value; NPV = negative predictive value; DW-MRI = Diffusion weighted magnetic resonance imaging

specificity of MRI were 99% and 99%, respectively. On the other hand, sensitivity and specificity of bone scan was 93% and 86%, respectively.[18] Another study reported that diagnostic accuracy of DW-MRI was significantly higher than bone scan (p<.05). The sensitivity and specificity of DW-MRI were 95.5% and 96.1, respectively.[19]

One more study documented that whole body MRI with DWI outperformed bone scan. The sensitivity of DWI-MRI was 62%, whereas, it was 91% for bone scan.[20] A Chinese study presented the sensitivity of DWI as 89.5%, specificity as 95.6%, PPV as 97.1%, and NPV as 60%, comparable to the findings of the present study.[21] Rezk et al. revealed that sensitivity, specificity, PPV, NPV, and diagnostic accuracy of DW-MRI for detecting bone metastasis were 82.1%, 78.0%, 85.2%, 74.0%, and 80.5%, respectively.[22]

The sensitivity and specificity of DW-MRI observed in this study were notable, particularly in the 22-40 years age group, where it exhibited a sensitivity of 70% and a specificity of 100%. In terms of disease duration, the findings suggest that DW-MRI performs better in detecting skeletal metastasis in patients with a shorter disease duration (<6 months), with a sensitivity of 82.6% and specificity of 78.5%. This was because bone lesions in early metastasis exhibit more distinct diffusion characteristics, which DW-MRI is particularly sensitive to. In contrast, patients with a longer duration of disease (>6 months) showed a drop in sensitivity (77.5%) and a slight increase in specificity (83%). This reflected the increased complexity and spread of metastases over time, making it more challenging for DW-MRI to detect all metastatic lesions accurately, especially in cases where the disease has become more diffuse or presents in less typical locations.

While DW-MRI showed considerable promise as a diagnostic tool for detecting bone metastasis in breast cancer patients, there are some limitations to be considered. The study population was relatively small, and further research with larger sample sizes is recommended to confirm the generalizability of these findings. Additionally, while DW-MRI does not involve ionizing radiation, it is not universally available in all clinical settings, and its implementation may require significant investment in advanced MRI technology. Despite these challenges, the results from this study suggest that DW-MRI has the potential to become a valuable complement to bone scans, offering greater diagnostic accuracy, especially in younger patients and those with early-stage metastasis. Lesions in breast and metastatic lymph nodes also showed moderate heterogeneous signals on DWI with corresponding low areas on ADC. Added advantage of breast lesion activity on DWI was helpful in detection of breast lesions which were difficult to characterize on imaging prior to biopsy.

Conclusion

Through the findings of this study, it is concluded that sensitivity and specificity values of DWIMRI are quite comparable with the findings on bone scan. DW-MRI can safely act as emerging modality for detection of skeletal metastatic lesions. Moreover, it has further advantage of assessing the treatment response after chemotherapy or radiation therapy along with additional details about breast lesions and metastatic lymph nodes. Scanning time for MR was variable according to number of sequences, however, it had relatively longer duration than bone scan. Advanced research is the need of hour to take management of progressed disease one step further towards better prognosis.

Ethical Approval: The Institutional Review Board, KEMU approved this study vide letter No. 322/ RC/ KEMU Dated 18-05-2024.

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Authors' Contribution:

NR: Conception & design, acquisition of data, drafting of article, critical revision for important intellectual content, final approval of the version to be published

SF: Analysis & interpretation of data, drafting of article, critical revision for important intellectual content

AM: Conception & design, acquisition of data, drafting of article

KSH: acquisition of data, drafting of article

FN: Analysis & interpretation of data, drafting of article

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