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Original

Sensitivity and specificity of nuclear medicines (DTPA and DMSA) with magnetic resonance imaging in diagnosing bone metastasis

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Abstract

Background: The frequency of bone metastases in individuals increases at advanced stages of cancer, mostly in patients suffering from lung, breast, or prostate cancer. The study aims to evaluate the effectiveness of bone metastases diagnosis of nuclear medicine, CT scan, and MRI in detecting bone metastases among patients with lung, breast, and prostate carcinoma.

Material and methods: Retrospective study design was adopted for the analysis of 120 recruited patients (with the presence of bone metastasis) following a series of examinations and tests.

Results: Better sensitivity (73.33%) and specificity (94.66%) for MRI as compared to SPECT. MRI also proved to be more sensitive (68%) and specific (95.74%), as compared to the findings of the CT scan.

Conclusions: The results conclude that MRI provided favorable diagnostic performance for bone metastasis. It emphasizes that diagnosis using MRI may enable practitioners to devise optimal carcinoma treatment strategies. The healthcare practitioners need to assess the MRI findings to determine improved treatment plans.

KEY words: bone; metastasis; magnetic resonance imaging; nuclear medicine

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Introduction

The process of metastasis is a debilitating property of a malignant tumor that is not confined to its origin site *i.e.*, the primary tumor site, but it can detach and spread to other parts of the body forming secondary tumors [1]. The formation of secondary tumors inside the bone or bone metastasis in a cancer patient is an incapacitating and often untreatable disease [2]. Halabi et al. [3] revealed an incidence of approximately 65–75% of skeletal involvement among patients with advanced cancer. After the lymph nodes, the skeleton is the second common malignancy site for the development of metastases from prostate or breast cancer. Mostly, the presence of bone metastases is implied to any alteration in an ongoing treatment, where survival prospects of the affected individual are low [4]. Complications such as spinal paralysis and pathological fractures caused by bone metastasis increase the complexity of the cancer treatment and pose a significant impact on an individual's quality of life [5]. Several studies have revealed that the diagnosis of bone metastases can have a substantial impact on the overall treatment strategy [3, 6].

The use of contemporary imaging techniques has enabled the rapid diagnosis of bone metastases. Nuclear medicine and magnetic resonance imaging (MRI) have a significant role in the diagnosis and therapy of bone metastases. The imaging of bone is considered one of the first nuclear medicine techniques. The sensitivity of nuclear medicine is 90 percent greater as compared to other imaging methods, particularly, when there is a compression of the spinal cord or inclusion of radiographic examination [7]. Whole-body MRI, axial skeleton MRI, and routine prostate/breast MRI are significant in the diagnosis of bone metastases [8]. The number of metastatic foci in the skeletal system is evaluated through suitable

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selected diagnostic imaging techniques, including positron emission tomography (PET), bone scintigraphy (BS), and whole-body MRI [9]. Whereas, according to Lukaszewski et al. [6], the extent of metastasis and its mixed, osteolytic, osteoblast characteristics are determined through complementary imaging examinations such as MRI, X-rays, and computed tomography (CT) scan.

One of the significant advantages of using MRI is the reporting of bone metastases response to treatment, using functional approaches, quantitative parameters, and morphologic images [10]. According to Qu, Huang at al. [11], compared to MRI or BS, PET scan was found more sensitive and specific in detecting bone metastasis due to lung cancer. Whereas, according to Huysse at al. [12], MRI has higher sensitivity compared to PET on a lesion level and has a low probability of false-negative results. Also, there is a predominant up-regulation of osteoblastic activity in bone metastases, which may lead to the formation of mineralized woven bone [13]. This condition shows a characteristic osteosclerotic appearance and is recognized as an osteoclast that plays a significant role in the pathophysiology of metastatic growth procedures [13]. The techniques, including nuclear medicine, CT scan, and MRI, can improve the diagnosis and check the response of therapy among cancer patients [6]. There is a strong need to evaluate and reveal the effectiveness of the mentioned techniques in detecting bone metastases in patients with lung, breast, and prostate carcinoma. This study significantly contributes by highlighting each modality's pros and cons, along with their response to treatment, and diagnoses of bone metastases. Additionally, it presents a practical approach for the evaluation of bone metastasis and the diagnosis of bone metastasis.

Nuclear medicines are widely used in approximately all the imaging techniques. But the diagnosis through this sometimes shows the false-negative results [14]. This misdiagnosis ultimately troubles the oncologist as well as the patient who does not understand the stage of bone metastases. Diethylenetriamine pentaacetate (DTPA) and dimercaptosuccinic acid (DMSA) are used with CT scans, and MRI and PET scanning. In the current study, both of these nuclear medicines were used in order to find their specificity and sensitivity in the diagnosis of bone metastases.

Although previous researchers have established the significance of digital imaging of bone metastasis in detecting and evaluating prostate, breast, and lung cancer; no empirical evidence is found concerning the agreement on the optimal imaging modality for detecting the specific disease. Union for International Cancer Control (UICC), response evaluation criteria in solid tumors, and World Health Organization (WHO) have developed the evaluation of bone tumor response criteria, but its execution was not found up to the mark in clinical practice and hence dissolved [15]. The comparison between nuclear medicines, DTPA and DMSA, with MRI for their specificity and sensitivity in detecting bone metastases has not been studied explicitly among prostate, lung, and breast carcinoma. The present study, therefore, bridges this gap and provides an evaluation of the quality parameters between different digital imaging systems and modalities of digital imaging systems. Mainly, it outlines the superiority of an imaging system over others concerning quality and sensitivity.

Materials and methods

Study design

This study is purely based on the retrospective design. The selection of this design is based on its efficacy for concluding effective results in previous studies [16, 17]. However, the present study differs from these studies in terms of its inclusion criteria, sample collection, and region. In this study, the patients with histologically proven malignancy but unknown bone metastasis were recruited. The patients were mainly diagnosed with prostate, lung, and breast carcinoma.

Study sample

The selection of the participants was based on the determining inclusion and exclusion criteria. Malignant patients who have the age 18 years or above were included in the study. The presence of bone metastasis was also one of the main factors that were ensured in the inclusion criteria. All the pregnant or lactating women were excluded from the study. Based on inclusion and exclusion criteria, a total of 120 patients were recruited for the study. The sample size was comparable to a similar study by Bafaraj [18]. Also, GPower 3.1 software was used to determine if the sample size comes within the estimated power analysis. It was calculated that at least 88 cases were required for 80% power with a 0.05 margin of error.

Data collection

Among these 120 patients, 37.5% were male, and the remaining 62.5% were female. These patients went through nuclear medicine scanning for the diagnosis of bone metastasis in them.

Study procedure

Diagnosis of metastasis, each patient was assessed for the presence of bone metastases using a series of examinations and tests. The presence was confirmed based on the application of MDP, MRI findings, and CT scan findings. For the CT scan, different angles of the patient's body were assessed, and cross-sectional images (slices) of the bones were created through computer processing. DTPA and DMSA are radioactive compounds that were used to perform scanning. MRI was performed using contrast material, typically gadolinium, which enhanced the appearance of certain details [19].

Measurement of sensitivity and specificity

Results obtained from the overall findings of each test were used to measure the sensitivity and specificity of each technique. In order to get the values of specificity and sensitivity, the results with true positive (TP), true negative (TN), false positive (FP), and false negative (FN) findings were isolated. Positive and negative predictive values were also obtained by using the obtained data [16].

Formula to measure the % sensitivity = $TP/(TP + FN) \times 100$

Formula to measure the % specificity = $TN/(TN + FP) \times 100$

Formula to measure the positive predictive value =

$= TP/(TP + FP) \times 100$

Formula to measure the negative predictive value =

$= TN/(TN + FN) \times 100$

Table 1. MRI Findings with diethylenetriamine pentaacetate (DTPA) and dimercaptosuccinic acid (DMSA)

Bone metastasis	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	p-value
DTPA	33	71	4	12	73.33%	94.66%	89.18%	85.54%	0.001
DMSA	34	67	3	16	68%	95.74%	68%	80.72%	0.001

TP — true positive; TN — true negative; FP — false positive; FN — false negative; PPV — positive predictive value; NPV — negative predictive value; DTPA — diethylenetriamine pentaacetate; DMSA — dimercaptosuccinic acid

Data analysis

All the examinations were observed following the administration of nuclear medicine. MRI scan was read in a standard workstation. The test was performed in segmental view. Data were analyzed through descriptive statistics using SPSS (Statistical Package for Social Sciences) Version 20.0. Pearson chi-square test was used to analyze the data for negative and positive cases. The results obtained from the interpretations were confirmed through clinical follow-up, histological evaluation, and other imaging studies.

Results

Table 1 shows statistically significant results for the detection of bone metastases through MRI using DMSA and DTPA. Sensitivity of DPTA and DMSA was 73.3% and 68% respectively which shows that the sensitivity of DPTA is significantly better than DMSA (p-value = 0.001). However, the specificity of both of these nuclear medicines was almost the same that is 94.66% and 95.74% (p-value = 0.001). Positive and negative predictive values were also obtained that show significantly higher PPV values of DTPA (89.18%) than DMSA (68%) (p-value = 0.001). NPV values were near in both of the scans *i.e.* DTPA and DMSA (85.54% and 80.72%). Overall, DTPA was found to be significantly better nuclear medicine compared to the DMSA which can be used in the diagnosis of bone metastasis with greater sensitivity and specificity.

Discussion

The study empirically reveals the sensitivity, specificity, and accuracy of two different nuclear medicines, DPTA and DMSA, with MRI scan through descriptive statistics. It found DTPA to be significantly more specific and sensitive in detecting bone metastasis. The sensitivity and specificity of MRI among cancer patients are more optimum as compared to any other imaging technique like CT/PET, BS, or SPECT findings [20]. As metastasis usually involves multiple sites and organs, therefore, a technique that does full-body imaging is more convenient and time-saving for patients [21]. Diethylenetriamine pentaacetate (DTPA) and dimercaptosuccinic acid (DMSA) are two different nuclear medicine that are used in the analysis of various organ functions and are widely used in the diagnosis of bone metastases of the whole body. DMSA and DTPA are also useful in the diagnosis of various organ function detection and show similar effects when used with CT or SPECT. The previous study shows that they exert no significant difference in imaging technique when doing renal scans, however, no study has compared their efficiency against each other in diagnosing bone metastasis [22]. These two nuclear medicines are very specific in the identification of bone metastases [23].

In this study, patients with prostate, lung, and breast carcinoma were enrolled. These tumors are widely found, and early and accurate diagnosis of these malignancies is a big challenge [24]. The present study would be helpful for such patients to know their metastatic stage earlier so that it can be managed accordingly. It is suggested that healthcare practitioners should assess the MRI findings with DTPA for determining improved treatment plans. However, consideration of the clinical setting and the clinical risk to the patients must also be studied for improved interpretation of the risk of bone metastasis.

The study was limited due to its retrospective nature. As the data were retrospectively collected, it was assumed that the scans and MRIs were done nearly at the same time. A similar prospective study on a larger population is suggested to have the diagnostic tests done nearly at the same time for more accuracy and a comparison with other modalities can also be done.

Conclusions

Magnetic resonance imaging (MRI) proves itself as the most accurate technique in the diagnosis and tumor and its metastases. This nuclear medicine made it more valuable in the identification. It is concluded that DTPA is more specific and sensitive in diagnosing bone metastases. The positive predictive value of DTPA is also greater than that of DMSA which also supports this finding. It provides clinical implication for using DTPA in detecting bone metastasis.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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