

Role of Bone Scintigraphy in Modification and Finalization of the Pathological Staging of Carcinoma of Breast

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ABSTRACT

Objectives: The prognosis and treatment planning of carcinoma depends upon the stage of the disease. The presence of bone metastasis affects a patient's prognosis and further treatment planning. The purpose of this study was whether bone scintigraphy by detecting skeletal metastasis can help in patient management by modification of initial pathological staging.

Patients and Methods: A total of 110 patients of breast carcinoma who were referred for the early bone scintigraphy after the surgical procedure were included in this study. Bone scintigraphy was done 3 hours after 15 mCi ^{99m}Tc methylene diphosphonate (MDP) intravenous injection. Images were acquired in Siemens E-cam dual head camera. Chi-Square test was used to analyze the variables

Results: Out of the total 110 patients with breast carcinoma referred to the institute after initial pathological staging nearly one third i.e. 31 (28.2%) patients had skeletal metastasis. In this study it was revealed that tumour size and nodal involvement correlated well with metastasis to bone. Skeletal metastasis was significantly ($p < 0.05$) higher in tumour size belonged to $>3.0 - \geq 5.0$ cm and nodal involvement N2-N3 ($p < 0.05$). Sixty eight of the patients were in pathological stage II, among them 22.1% of the patients had skeletal metastasis. Pathological stage III was observed in 33 cases, among them 48.5% patients had skeletal metastasis and as thus staging was modified by bone scintigraphy in 22.1% in stage II and 48.5% in stage III. Pathological stage I was in 9 cases among them no metastasis was observed.

Conclusion: Bone scintigraphy is a useful imaging modality in staging of breast carcinoma. It is recommended in patients with stage II and above and this can influence the clinical management.

Key words: Bone scintigraphy, breast cancer and pathological staging.

INTRODUCTION

Breast cancer is one of the common diseases among the females in the world. Generally more than 25% women are affected by breast cancer, in that 20% leads to lethal cancers. It is one the leading cause of death due to

cancer in women. It forms in tissues of breast, usually ducts and lobules (1). It is a disease that commonly metastasizes to bone and increasing morbidity, mortality and health service cost (2). Bone is the most common site of first distant relapse (3). Extent of bone metastasis correlates well with tumour size (T), lymph node involvement (N) and histopathology.

^{99m}Tc MDP bone scintigraphy historically has played a significant part in the evaluation of skeletal disease and continues to be one of the most clinically utilized investigations in the staging and follow-up of breast cancer patients (2). Staging that is the extent of spread at presentation is one of the most important prognostic factors for breast cancer patients (4). Determining the presence of metastasis both at presentation and after initial treatment is a key factor in optimal diagnosis and determining ongoing treatment (5). The ^{99m}Tc MDP has been also shown to find the extent of tumor in patients in whom breast cancer is present (6). The incidence of breast cancer metastasis to bone is high, however many reports have shown that patients with stage I or II breast cancer have a lower probability of having bone metastasis in staging studies, indicating little benefit for these patients from the bone scan for staging of the disease (7,8). However, other authors have reported that patients with large stage II tumors or high-grade histopathology require staging by bone scintigraphy (9). Although most physicians accept the idea that staging by bone scintigraphy of stage I breast cancer patients yields little clinically useful data, others

regard it as a valuable diagnostic tool at any stage (10). The more recent developed diagnosis imaging techniques such as CT and nuclear magnetic resonance (NMR) although helpful in study of bones lesion may not be used in all patients with respected metastasis disease. Bone scan is highly sensitive for the detection of skeletal metastasis; it can image the entire skeletal at a time at reasonable cost. Therefore, bone scan remains popular despite technological advance in magnetic resonance imaging (MRI), computed tomography (CT) & PET (11). The sensitivity for detecting metastatic disease is often quoted as high as 95% or above. It can diagnose metastasis at an early stage even when there is no symptom. Therefore this study is designed to establish that bone scintigraphy is a useful imaging modality in staging of breast carcinoma.

PATIENTS AND METHODS

This observational type of study was carried out in National Institute of Nuclear Medicine & Allied Sciences (NINMAS), during July 2014 to June 2015. A total of 110 patients of breast carcinoma referred for the first time bone scintigraphy after surgical procedure were included in this study. Bone scintigraphy was done after 3 hours of 15mci 99mTc MDP intravenous injection. Images were acquired in Siemens E-cam dual head camera. Chi-Square test was used to analyze the variables. A P-value was considered to be statistically significant if ≤ 0.05 and statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Among the total 110 patients of breast carcinoma, most of them presented with size of tumour belonged to 2.1-3.0 cm, lymph node stages N1 followed by N0, N2 and N3. Almost one third (28.2%) patients had skeletal metastasis, among them 7 (22.6%) patients had solitary metastasis and 24 (77.4%) had multiple metastases (Table 1). In this study it was revealed that

tumour size and nodal involvement correlated with metastasis to bone. Skeletal metastasis was significantly ($p < 0.05$) higher in pathological tumour parameter belonged to $>3.0 - \geq 5.0$ cm and nodal involvement N2-N3 ($p < 0.05$) (Table 2,3). Majority of the patients were in pathological stage II, and 22.1% patients had skeletal metastasis. Pathological stage I was in 9 cases and no metastasis was observed. Pathological stage III was observed in 33 cases, among them 48.5% patients had skeletal metastasis (Table 4). Thus staging was modified by bone scintigraphy in 22.1% in stage II and 48.5% in stage III (Table 5).

Table 1: Distribution of patients by pattern of skeletal metastasis (n=31)

Skeletal metastasis	Number of patients	Percentage
Solitary	7	22.6
Multiple	24	77.4

Table 2: Association between skeletal metastasis status with pathological tumour parameter (n=110)

Pathological tumour parameter (cm)	Skeletal metastasis status				P value	
	Present (n=31)		Absent (n=79)			
	n	%	n	%		
<2.0- \leq 3.0	88	20	22.7	68	77.3	0.011 ^s
>3.0- \geq 5.0	22	11	50.0	11	50.0	

s= significant
P value reached from chi square test

Table 3: Association between skeletal metastasis status with pathological nodal involvement (n=110)

Pathological nodal involvement	Skeletal metastasis status				P value	
	Present (n=31)		Absent (n=79)			
	n	%	n	%		
N0-N1	85	18	21.2	67	78.8	0.003 ^s
N2-N3	25	13	52.0	12	48.0	

s=significant
P value reached from chi square test

Table 4: Association between metastasis status with pathological stages (n=110)

Pathological stages	Present (n=31)			Absent (n=79)	
	N	no	%	no	%
I	9	0	0.0	9	100.0
II	68	15	22.1	53	77.9
III	33	16	48.5	17	51.5

Table 5: According to pathological staging modification to stage IV

Stage I	0.0%
Stage II	22.1%
Stage III	48.5%

DISCUSSION

Worldwide, breast cancer is the most common cancer and constitutes the leading cause of cancer death among women (12). Most of the cases are diagnosed in advanced stages because of lack of awareness and screening. In this study it was observed that 36 (32.7%) patients belonged to age 30-39 years, 34 (30.9%) belonged to age 40-49 years, 16 (14.6%) belonged to age 21-29 years 2 (1.8%) belonged to age ≤ 20 years, and 4 (3.6%) patients belonged to age ≥ 70 years. Similarly, Ahn et al. showed 80.0% patients with carcinoma of breast belonged to age ≥ 35 years (13). In developed countries, 75% of all breast carcinomas occur in postmenopausal women, of which about 80% are hormone receptor positive (14). The apparently higher incidence of breast carcinoma in younger age may be due to geographical variations, racial, ethnic differences, genetic causes, different lifestyle and increased life expectancy of the women. Regarding pathological tumour and nodal parameter it was observed that tumour belonged to $<2.0- \leq 3.0$ cm in 88 cases, among them 22.7% had skeletal metastasis, tumour $>3.0- \geq 5.0$ cm was found in 22 cases, among them 50.0% had skeletal metastasis.

Skeletal metastasis was significantly ($p < 0.05$) higher in tumour parameter belonged to $>3.0- \geq 5.0$ cm (Table 2). In pathological nodal involvement (N0-N1) found in 85 cases, among them 21.2% patients presented with skeletal metastasis, N2-N3 found in 25 cases, among them 52.0% had skeletal metastasis. Skeletal metastasis was significantly ($p < 0.05$) higher in pathological nodal involvement in N2-N3 (Table 3).

Bone scintigraphy is highly sensitive for the detection of skeletal metastasis; it can image the entire skeleton at a time at reasonable cost. In this current study it was observed that 28.2% patients had skeletal metastasis, among them 22.6% patients had solitary and 77.4% had multiple metastases (Table 2,3). Similarly, Ahn et al. showed multiple metastases were in 70.9%, which is closely resembled with the present study (13).

In this study it was observed that majority of the patients (68) had pathological stage II, among them 22.1% patients had skeletal metastasis. Pathological stage III was observed in 33 cases, among them 48.5% patients had metastasis. Koizumi et al. reported that the incidence of metastasis to bone was 0% in pathological stage 0 and I, 0.64% in stage II, 7.25% in stage III and 13.73% in stage IV (15). Myers et al. documented that out of 350 patients analyzed 133 had stage I, 188 were stage II and 37 were stage III disease. Bone scintigraphy was performed on 94.7% patients and was positive for metastases in only 0.9% of stage I and II patients but was positive in 16.2% of patients with stage III disease (5).

There are significant variations in outcomes of early breast cancer among different regions, as the burden of metastatic breast cancer (MBC) may differ from that of early disease. There is however, a major lack of accurate data on this prevalence in the great majority of countries since most cancer registries do not capture relapses (16). Despite recent widespread patient screening advances as well as heightened health awareness, a significant proportion of women still present with advanced breast carcinoma. In

women with pathological stage I tumour extensive staging investigations may be avoided, but women who have pathological stage II bone scan is recommended as part of staging (5) and positive bone scan in stage II disease have influenced the clinical management of the patient (17). In this study by bone scintigraphy pathological staging is modified in 22.1% in stage II and 48.5% in stage III respectively which may modify the planning of management (Table 10). Early detection and treatment of bone metastasis in breast carcinoma patients give better prognosis, as it is possible to eradicate asymptomatic metastasis demonstrated by bone scintigraphy by commencing treatment at an early stage.

CONCLUSION

This study was undertaken to evaluate the role of bone scintigraphy for modification and finalization of initial pathological staging of carcinoma of breast. In this study skeletal metastasis found in pathological stage II and stage III 22.1% and 48.5% respectively which modified the staging of breast carcinoma but in stage I no skeletal metastasis was observed. So staging by bone scintigraphy is recommended in patients with stage II and above and this can influence the clinical management.

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