

Role of bone scan in newly diagnosed breast cancer patients in Erbil City

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Abstract:

Background and objectives: It is necessary to highlight the importance of general nuclear medicine in the care of women with breast cancer including detection, classification and treatment guidance, accordingly this study was conducted to investigate the role of bone scan among newly diagnosed breast cancer patients and to find out the relationship between some clinico-pathological variables and bone metastasis.

Methodology: This retrospective study was done in Nuclear Medicine unit- the radiological department of Hawler teaching hospital in Erbil City in which 40 confirmed breast cancer cases referred from various hospitals in Erbil were included in the study. Statistical Package for Social Science was used for the purpose of data analysis.

Results: The age of breast cancer patients ranged from 26 to 59 years, with a mean age \pm SD of 44.8 ± 8.88 years. The majority (90%) were clinically presented with signs of a lump in the breasts. 62.5% of them had lymph node involvement, and the majority (95.0%) showed ductal carcinoma. Abnormal bone scan findings were identified among 42.5% of them, especially among those with stage II, advanced age, more lymph node involvement, and a sensitivity of 47.0%, and specificity of 60.9%. Multiple skeletal metastases were found most commonly in the ribs and lower limbs (67.0% and 64%, respectively). Most of the socio-demographic and clinical factors revealed non-definitive associations with the bone scan findings.

Conclusions: The quality of the imaging findings was not encouraging, because of relatively low sensitivity and specificity, accordingly for each patient; the right investigative technique should be selected individually, taking into consideration different clinico-pathological features of the patients.

Keywords: diagnosed breast cancer, retrospective study, Erbil city

Introduction:

Breast cancer is the most commonly diagnosed cancer and the important cause of cancer-related mortality among women worldwide, with an increasing incidence in many areas of the world.^{1,2} Globally, a 20% increase in frequency

and 14% rise in mortality since 2008 support clinical approaches that both decrease risk and enhance prompt management including early detection and treatment.³

It is necessary to highlight the importance of general nuclear medicine in the care of women with breast cancer including detection, classification (benign vs. malignant), treatment guidance, monitoring cardiotoxicity from different therapeutic procedures and evaluating the disease progression or recurrence, and bone scan has been the standard method for nuclear imaging of the skeletal system for decades.^{4, 5}

Metastases to bone is more common than primary bone malignancies and it is the third most common organ affected by metastasis, after the lungs and liver.⁶ Almost all types of cancer may metastasize to bone, especially those arising from breast, lungs, prostate, kidneys, and thyroid. The pelvis, vertebrae, ends of long bones and ribs, are the commonest sites of metastases because of its high red marrow content.⁷⁻⁹

Bone metastasis is so common in breast cancer and affecting nearly 70% of patients and radioisotope bone scintigraphy is considered as the most accurate and common technique for screening bony metastasis.¹⁰⁻¹²

Therefore, early detection of bone metastases is a crucial step for proper staging, choosing the best treatment strategy, and to reduce the possibility of complications and improving patients' quality of life.^{6, 7} Up to the researchers knowledge there are scarce data and researches addressing role of bone scan in early detection of bone metastasis among breast cancer patients, and due to the increasing prevalence of breast cancer, especially among females in our community, this study was conducted to investigate the role of bone scan among early diagnosed breast cancer patients in Erbil City and to find out the relationship between some clinico-pathological variables and bone metastasis.

Patients and methods:

This retrospective study was done in Nuclear Medicine unit- the radiological department of Hawler Teaching Hospital in Erbil City of Iraqi Kurdistan Region, where the patients' records were reviewed from the period of January 2009 to the end of December 2010. This study included 40 newly diagnosed breast cancer cases referred from various hospitals in Erbil. The inclusion criteria included all the newly diagnosed patients with positive breast cancer within the first 3 months of their histo-pathological diagnosis, and patients received or didn't receive radiotherapy or chemotherapy. Those with a history of recent intake of radiotracer materials, pregnant patients and those with metastases breast cancer previously diagnosed by bone scan were excluded from the study.

Bone scintigraphy was performed for all the patients using ^{99m}Tc-MDP as a bone-seeking agent given intravenously at a dose of 740 - 1110 MBq (20 - 30 mCi), imaging done after 2 - 4 hours of tracer injection by a double detector SPECT dual detector Gamma Camera using low energy with a high-resolution collimator.

Anterior and posterior whole-body bone images were obtained with the patient lying supine scanned from head to foot, over a period of 20 - 40 minutes and to study a particular part of the body in more detail a special kind of bone scan, called Single Photon Emission Computed Tomography (SPECT) image was used that usually took an additional 30 - 45 minutes, (or even more) to completely define the location and extent of any questionable abnormality, especially in the skull and the spines.

Interpretation of the bone scintigraphy images was done by nuclear medicine physician and abnormalities were recorded accordingly and the scintigraphy was read as suggestive of metastatic breast cancer or negative for metastases.

An abnormal bone scan (with or without associated area of radiographic normality or evidence of metastases) was considered positive for metastases and normal bone scintigraphy or bone scan abnormality not suggestive of metastases (benign bone disease) associated with a benign radiographic finding was considered negative for metastases. The study protocol was approved by the scientific committee of Erbil Polytechnic University. The collected data were subjected for appropriate statistical analysis using computer-based software (SPSS for Windows version 17.0) to compute mean, standard deviation, frequency tables and Chi square and Fischer's exact test to analyze categorical variables, considering P value ≤ 0.05 as statistically significant.

3. Results:

Clinical profile of breast cancer patients:

A total of 40 patients with breast cancer were enrolled in the current study; their age ranged from 26 to 59 years, with a mean age \pm SD of 44.8 ± 8.88 years. The majority (90%) were clinically presented with signs of a lump in the breasts, with more involvement (57.5%) of the right breast. Around two-thirds (62.5%) of them had lymph node involvement, and the majority (95.0%) showed ductal carcinoma by histo pathological examination, (Table 1).

Table 1: Clinical profile of breast cancer patients

Variable	No. (%)
Clinical presentation	
Lump	36 (90.0)
Axillary Lymph node enlargement	3 (7.5)
Discharge	1 (2.5)
Involved side of the breast	
Right breast	23 (57.5)
Left breast	15 (37.5)
Bilateral	2 (5.0)
Lymph node involvement by histopathology	
Involved	25 (62.5)
Not involved	15 (37.5)
Histo pathological findings	
Ductal carcinoma	38 (95.0)
Lobular carcinoma	2 (5.0)
Total	40 (100)

Sensitivity and specificity of the bone scan:

The study revealed that the sensitivity of bone scan was 47.0%, with a specificity of 60.9%. (Table 2).

Table 2: Sensitivity and specificity of the bone scan

Bone scan	Skeletal metastasis		Total
	Abnormal	Normal	
Abnormal	8	9	17
Normal	9	14	23
Total	17	23	40

Relationship of tumor stages and skeletal metastasis with radiological findings (Bone scan):

Regarding tumor stages of the breast cancer patients, almost more than half (57.5%) of the patients were presented with stage II, followed by stages III and I (22.5% and 17.5%, respectively). However, more abnormal bone scan findings were found among those with stage II of the disease with no significant statistical association ($P= 0.122$). Abnormal bone scan findings were identified among 42.5% of the patients with no significant statistical association between bone scan findings and skeletal metastasis ($P= 0.479$), (Table 3).

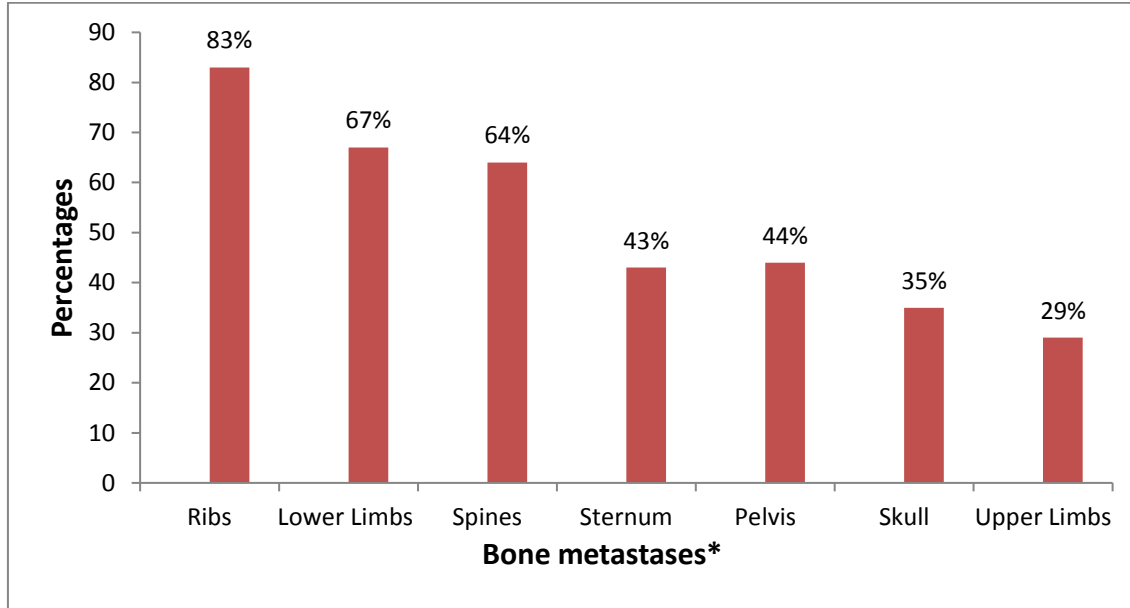
Table 3: Relationship of tumor stages and skeletal metastasis with radiological findings (Bone scan)

Variables	Bone scan findings		Total *	P value
	Normal	Abnormal		
Tumor staging				
Stage I	2 (28.6)	5 (71.4.4)	7 (17.5)	0.122**
Stage II	16 (69.6)	7 (30.4)	23 (57.5)	
Stage III	4 (44.4)	5 (55.6)	9 (22.5)	
Stage IV	1 (100.0)	0 (0.0)	1 (2.5)	
Skeletal metastasis				
Normal finding	14 (60.9)	9 (39.1)	23 (57.5)	0.749
Abnormal finding	9 (52.9)	8 (47.1)	17(42.5)	
Total	23 (57.5)	17 (42.5)	40 (100.0)	

*: Column percentage
**: Fischer`s exact test

The common sites of skeletal metastasis:

Results of bone scan showed that the breast cancer patients had multiple skeletal metastases, and most common site was in the ribs among 83% of them followed by metastasis to lower limbs and spines (67.0% and 64%, respectively) and the least metastasis (29.0%) was to the upper limbs, (Figures 1 & 2).



*: Breast cancer patients had multiple skeletal metastases

Figure 1: Results of bone scan showing common sites of skeletal metastasis

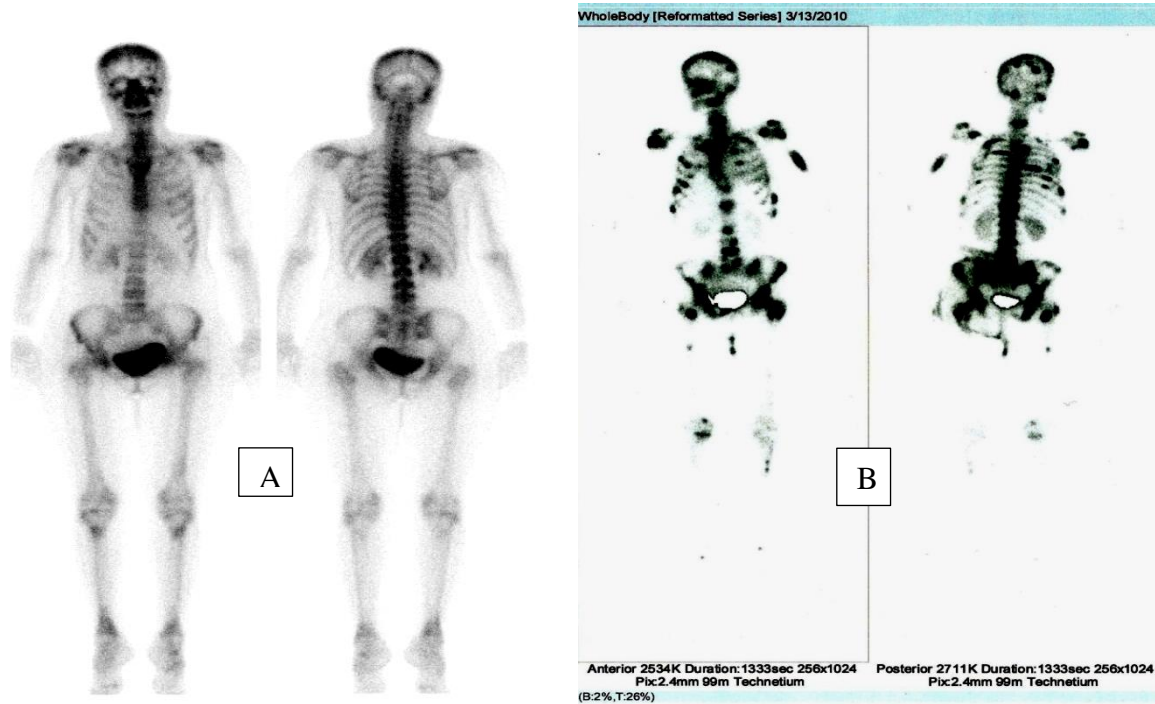


Figure 2: Whole body bone scan showing A. Normal body scan. B. Multiple bone metastases in breast cancer patient.

Association of the clinical presentation of breast cancer and lymph node involvement to the skeletal metastasis:

Breast cancer patients with advanced clinical stage of the disease had significantly ($P= 0.001$) more metastasis compared to those with an early invasive stage. Also, those with lymph node involvement had significantly ($P= 0.007$) higher metastasis rate compared to those with no lymph node involvement, (Table 4).

Table 4:Association of the clinical presentation of breast cancer and lymph node involvement to the skeletal metastasis.

Variables	Skeletal metastasis		Total *	P value **
	No metastasis	Metastasis		
Clinical presentation of breast cancer patients				
Early invasive	19 (79.2)	5 (20.8)	24 (60.0)	0.001
Advanced	4 (25.0)	12 (75.0)	16 (40.0)	
Lymph node involvement				
Not involved	13 (86.7)	2 (13.3)	15 (37.5)	0.007
Involved	10 (40.0)	15 (60.0)	25 (62.5)	

Total	23 (57.5)	17 (42.5)	40 (100.0)
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*: Column percentage
 **: Fischer`s exact test

Relation of Socio-demographic characteristics of breast cancer patients to skeletal metastasis:

Among the breast cancer patients, 50% of them were aged between 40-49 years, with no significant statistical association between age groups of the patients with skeletal metastasis ($P= 0.216$). Also, there was no significant statistical association between other socio-demographic characteristics (Including marital status, family history of breast cancer, ... and breast feeding) of breast cancer patients and skeletal metastasis, (Table 5).

Table 5: Association of the Socio-demographic characteristics of breast cancer patients to skeletal metastasis:

Variables	Skeletal metastasis (Bone scan)			Pvalue **
	No metastasis	Metastasis	Total *	
Age groups				
≤ 39 years	6 (75.0%)	2 (25.0%)	8 (20.0)	0.216
40- 49 years	10 (50.0)	10 (50.0)	20 (50.0)	
≥ 50 years	7 (58.3)	5 (41.7)	12 (30.0)	
Marital status				
Married	18 (52.9)	16 (47.1)	34 (85.0)	0.535
Single	5 (83.3)	1 (16.7)	6 (15.0)	
Family history of breast cancer				
Negative	23 (60.5)	15 (39.5)	38 (95.5)	0.174
Positive	0 (0.0)	2 (100.0)	2 (5.0)	
Educational status				
Illiterate	6 (41.7)	4 (58.3)	10 (25.0)	0.794
Primary school education	7 (46.7)	8 (53.3)	15 (37.5)	
Secondary school education	8 (66.7)	4 (33.3)	12 (30.0)	
Higher education ***	2 (66.7)	1 (33.3)	3 (7.5)	
Monthly Family income				
Sufficient	5 (41.7)	7 (58.3)	12 (30.0)	0.549
More than sufficient	4 (66.7)	2 (33.3)	6 (15.0)	
Less than sufficient	14 (63.6)	8 (36.4)	22 (55.0)	

Smoking				
Yes	6 (75.0)	2 (25.0)	8 (20.0)	0.428
No	17 (53.1)	15 (46.9)	32 (80.0)	
Breastfeeding				
Yes	10 (47.6)	11 (52.4)	21 (52.5)	0.216
No	13 (68.4)	6 (31.6)	19 (47.5)	
Total	23 (57.5)	17 (42.5)	40 (100.0)	

*: Column percentage **: Fischer`s Exact Test***: Diploma, B.Sc. & Postgraduate degrees

4. Discussion:

Breast cancer is one of the common malignancies in Iraq, accounting for one-third of all registered female cancers. Nearly 30% of patients with early-stage breast cancer develop metastases, however, metastatic breast cancer occurs in 6- 7% of newly diagnosed breast cancer patients.¹³The imaging technique plays a significant role in preoperative assessment, treatment efficacy estimation and monitoring progress of bone metastases.⁴

In the current study, the majorities were clinically presented with signs of a lump in the breasts; this is in contrast to the results of a study in Italy, where 56.25% of the breast cancer patients were presented with lymph node involvement.¹⁴In this study around two-thirds of them had lymph node involvement, and the majority showed ductal carcinoma by histo-pathological examination. Almost similar results were found in a WHO report and a study in Turkey, where ductal carcinoma was the major predominant histo-pathological findings.^{15, 16} Age of the patient is an important factor both for the disease occurrence and management, whereas 95% of all new breast cancer cases evolving among females aged 40 years or older.¹⁷ Also, our result was consistent with other studies in Iraq, which showed that the peak frequency was recorded in the age period of 40-49 years.¹⁸ This could be attributed to the age of the patients that have been found to be a risk factor for developing breast cancer worldwide, where 75% of new cases and 84% of breast cancer deaths occur in women aged 50 years and older.^{15, 19}

The sensitivity of bone scan was 47.0%, with a specificity of 60.9%, this was inconsistent with results of a study in Germany, where the sensitivity and specificity of bone scanning was higher (81% and 86%, respectively).⁸ Studies in USA and Brazil showed low sensitivity and high specificity of the bone scan.^{17, 20} Although bone scintigraphy (bone scan) is considered to be a non-specific tool, but usually considered as a good and efficient method for initial evaluation and follow-up of bone metastases. Also, type of the equipment, quality of the used radioactive materials and experience of the nuclear medicine specialist could play a role in determining sensitivity and specificity of bone scan.

In our study, almost more than half of the breast cancer patients were presented with stage II, followed by stages III and I. However, more abnormal bone scan findings were found among those with stage II of the disease with no significant statistical difference. Almost similar results were found in a study in China and Brazil. The Brazilian study revealed that 7 (14.5%) patients were Stage I, 14 (29.1%) stage II, 18 (37.5%) stage III and 9 (18.7%) stage IV with no correlation between breast cancer clinical staging and the other parameters.^{20,21} However, a study in Korea revealed a significant difference in the bone metastasis rate between patients with different disease stages ($P = 0.039$).²² This could be due to the fact that malignancies which are presented with advanced clinical stages, it is not necessary to

show more obvious clinical signs, multiple lesions or tendency to localize in the skeleton.

In this study, there was no significant statistical association between bone scan findings and skeletal metastasis ($P=0.479$). Almost similar results were reported in a study in Iran, where there was no statistically significant relation in histo-pathologic type between breast cancer patients with or without bone metastasis.²³

In this study, results of bone scan showed that the breast cancer patients had multiple skeletal metastases, and most common site was in the ribs among 83% of them followed by metastasis to lower limbs and spines (67.0% and 64%, respectively) and the least metastasis (29.0%) was to the upper limbs. Studies in China and USA revealed that the incidence of bone metastases among breast cancer patients was 15.3%, and the most common sites of bone metastases were spines, followed by ribs and pelvis.^{21, 24} Bone is the most frequent site of distant metastasis from breast cancer and accounts for the highest proportion of first site relapse in patients with breast cancer.

In this study breast cancer patients with advanced clinical stage of the disease had significantly ($P=0.001$) more metastasis compared to those with an early invasive stage. Almost similar results were found in a study in Korea, they found a significant difference in the bone metastasis rate between patients with different stages of the disease ($P=0.039$).²² Also, those with lymph node involvement had significantly ($P=0.007$) higher metastasis rate compared to those with no lymph node involvement. Almost similar results were found in a study in Japan, where clinical staging ($P<0.0001$), and the number of lymph node involvement ($P=0.0029$), were independently significant risk factors for bone metastases.²⁵ Another study in China revealed that significantly higher rates of bone metastasis were detected in patients with multiple lesions, and more lymph node involvement.²¹ The more advanced stages of breast cancer with more lymph node involvement carries more possibilities for bone metastases, which is the case in most developing countries where most of breast cancer patients are presented in late stages with higher skeletal metastasis.¹⁰⁻¹²

Among the breast cancer patients, half of them were aged between 40-49 years, with no significant statistical association between age groups of the patients and skeletal metastasis. Almost similar results were reported in a study in Iraq, where the peak incidence of breast cancer was observed among patients in 5th and 6th decades of life.²⁶ This could be attributed to the age of the patients that have been found to have risk factors for developing breast cancer worldwide. Also, there was no significant statistical association between other socio-demographic characteristics (Including marital status, family history of breast cancer.... and breastfeeding) of breast cancer patients and skeletal metastasis. While a study in Portugal showed that most of the clinico-pathological, genetic, and metabolic factors revealed conflicting or non-definitive associations and could not be validated for clinical use.¹⁹

This is the first study in Erbil and Kurdistan region that addresses the role of bone scanning in the diagnosis of breast cancer patients with certain emphasis on risk factors for skeletal metastasis.

This study had certain limitations; first, the data was collected from single institutional reports. Second, there were problems with the radioactive material supply during the study period; the equipment used was not so updated and sensitive. Accordingly, all these factors mentioned above had negatively affected patients registration and follow up.

In conclusion, the study had concluded that the breast cancer patients had multiple skeletal metastases, and the most common site was in the ribs with relatively low sensitivity and specificity of the bone scan. Patients being in the 5th decade of life, advanced stages of the disease with more lymph node involvement carry more possibility for skeletal metastasis.

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