Original Article

Opportunistic use of "follow-up" chest and abdominal computed tomography in the assessment of bone mineral density of breast cancer patients in a resource-poor nation

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Abstract

Background: Breast cancer patients experience bone loss from treatment-induced menopause, as well as from the direct effect of cancer. The use of computed tomography (CT) attenuation values of the lumbar spine to estimate bone mineral density has been validated by several studies.

Materials and Methods: This was a retrospective study conducted at Sweden Ghana Medical Centre and Korle Bu Teaching Hospital between June 2016 and August 2019. Measurement of Hounsfield unit (HU) of lumbar vertebrae was achieved by drawing an elliptical region of interest (ROI) on an axial image of the vertebra about 2–3 mm from the spinal cortical bone. The mean HU of the ROI was measured on bone window for each of the vertebral bodies, and the values were documented and analyzed.

Results: The mean bone densities of the vertebrae were generally higher for the noncancer patients compared to the breast cancer patients for all the age groups. The measured bone densities showed a normal distribution curve. The range of bone density for osteopenia and osteoporosis was between 174.4 and 236.4 HU and <174.4 HU, respectively. A Pearson's correlation analysis between patient age and bone density for both groups showed a negative statistically significant relationship.

Conclusion: Using CT attenuation values of lumbar vertebra to estimate bone density established that the bone densities follow a normal distribution, the mean bone density for breast cancer patients were slightly lower than for noncancer patients, and age correlated better with lumbar bone density in noncancer patients than in breast cancer patients.

Keywords: Bone density, breast cancer, computed tomography, Hounsfield unit

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INTRODUCTION

Breast cancer patients experience bone loss from the direct effect of cancer and chemotherapy and indirectly from treatment-induced menopause.[1-3]

Bone mineral density (BMD) estimation by dual-energy X-ray absorptiometry (DEXA) can predict an individual's risk of developing osteoporosis.[4-6]

Computed tomography (CT) estimated attenuation values of the lumbar spine can serve as an index of BMD. This has been validated by several studies using abdominal and chest CT scans that were ordered for other reasons.[5,7-9]

This study aims to validate the use of measured Lumbar CT attenuation values to monitor BMD in breast cancer patients in an environment where DEXA is unavailable.

MATERIALS AND METHODS

This was a retrospective study conducted at Sweden Ghana Medical Centre (SGMC), an oncology center, and Korle Bu Teaching Hospital (KBTH), the largest tertiary hospital in Ghana. The subjects of the study were all females and made up of two groups. The first group comprised breast cancer patients with early disease (Stage I and II) who had been seen at SGMC between June 2016 and August 2019 and had undergone at least one chest or abdominal CT scan study after initiation of their treatment. Their clinical information and CT scan images were used for the study. This group of patients was referred to as the cancer group.

The second group was females who did not have cancer at the time of the study but had chest and/or abdominal CT scan at the Radiology Department of KBTH for nonmalignant conditions were referred to as the noncancer group. Their demographic information and CT scan images were also used for the study. This group of patients was used as controls and selected to match the ages of the cases.

Both sets of patients had blood creatinine levels evaluated and were fit to undergo contrast studies. Patients with significant renal impairment were excluded from this study.

Thoracic and abdominal CT scan images of the patients from both SGMC and KBTH were reviewed by a senior radiologist to rule out evidence of metastasis. Following this, the Hounsfield units (HUs) of L1–L3 vertebral bodies were measured and documented. RadiAnt DICOM Viewer-a software made by Medixant, Poznan, Poland: Medixant Promienista 25, 60-288 Poznań. Poland and Merge PACS: A product of IBM, Armonk, New York, United States: 1 New Orchard Road Armonk, New York 10504-1722, United States for viewing DICOM images were used to evaluate the images and to measure the HU at SGMC and KBTH, respectively.

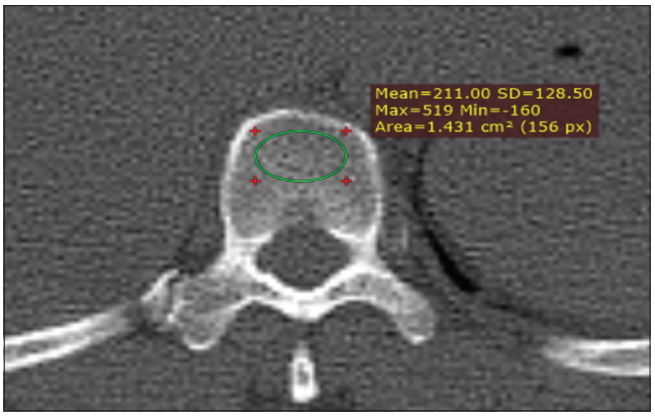

Figure 1: Measurement of Hounsfield Unit

Measurement of Hounsfield unit of lumbar vertebrae

This was done using the methods described by Budroff *et al*., Emohare *et al*., and Pickardt *et al*.[4,8,10] The lumbar vertebrae were viewed in the axial plane using both bone and soft tissue windows to rule out any significant pathology. An elliptical region of interest (ROI) was drawn at the center of the vertebra about 2–3 mm from the spinal cortical bone [Figure 1] Some areas such as the cortical bone and where large vessels pass on the posterior aspect of the vertebral body, bone island, fractures, and calcified herniated disks were excluded from the ROI. The mean HU of the ROI was measured on bone window for each of the vertebral bodies and the values documented.

Data analysis

Information was collected and cleaned on an MS excel spreadsheet and analyzed using Statistical Package for the Social Sciences: A product of IBM, Armonk, New York, United States (1 New Orchard Road Armonk, New York 10504-1722, United States) in a password-protected computer.

1. The mean HU for females aged 20–30 was used as a reference mean HU. Mean HU for each vertebra was reported as mean ± standard deviation (SD). Using the reference, a T-score was obtained using the formula T-score = (HU-ref (mean))/ref (SD). This was used to determine a reference HU for osteopenia and osteoporosis in the sample population using the WHO definition of these conditions[5,11]
2. The mean HU for the various age groups of the controls and for the cases were compared using paired sample *t*-test to find out if there was any difference in

the HU and whether the difference was significant

3. Correlation analysis was performed to find out the relationship between bone density of L1 vertebra and age for the cancer group and noncancer groups.

L1 vertebra was used as a representative for L1–L3 vertebrae because its density was assessed in all the patients. For some of the patients who had only chest CT scan, their L2 and L3 vertebral bodies were not imaged hence could not be evaluated.

Ethical issues

Ethical approval was obtained from the Institutional Review Board of KBTH. Confidentiality of patient information obtained from the hospital records and the imaging findings was ensured. Permission was also sought from the management of SGMC to use the information for this study.

RESULTS

A total of 158 breast cancer and 163 noncancer patients were recruited for the study with ages ranging from 27 to 82 and 21–84 years, respectively. The mean age of the control and cases were 49.4 ± 11.8 years and 47.9 ± 14.2 years, respectively, as shown on Table 1. The differences between the mean ages were significant ($P = 0.000$).

The mean bone densities of the L1–L3 vertebrae were generally higher for the control patients compared to the breast cancer patients for all the age groups except those >60 years as shown in Table 2. There was however no significant difference ($P = 0.214$) between the mean bone density for both groups.

The bone densities as measured by the HU showed a normal distribution curve with that for L1 vertebra as shown in Figure 2. The mean bone density for both cancer and noncancer patients was 212.95 HU with a standard deviation of 62.60 HU.

A Pearson's correlation analysis between patient age and bone density for cancer and noncancer group showed a negative statistically significant relationship with a

Table 1: Mean age of the various age-groups

Age group	Mean	*n*	SD
20-29			
No cancer	26.71	21	3.180
Cancer	28.00	2	1.414
30-39			
No cancer	35.50	34	3.116
Cancer	35.69	32	2.117
40-49			
No cancer	44.81	31	3.114
Cancer	43.83	48	2.563
50-59			
No cancer	53.71	38	2.629
Cancer	53.78	49	2.084
60-90			
No cancer	67.00	39	5.501
Cancer	69.11	27	7.433
Total			
No cancer	47.92	163	14.203
Cancer	49.39	158	11.822

n – Number of subjects in each group; SD – Standard deviation

Table 2: Mean bone density of the various age groups

Age group	Bone density-L1 vertebra	Bone density-L2 vertebra	Bone density-L3 vertebra
20-29			
No cancer			
Mean	277.77	288.89	288.37
n	21.00	18.00	14.00
SD	41.37	51.70	42.27
Cancer			
Mean	229.36	248.33	235.53
n	2.00	2.00	2.00
SD	77.41	56.30	28.60
30-39			
No cancer			
Mean	262.02	314.86	241.68
n	34.00	30.00	23.00
SD	42.66	300.04	54.02
Cancer			
Mean	258.94	267.28	262.63
n	32.00	32.00	31.00
SD	37.24	44.97	44.65
40-49			
No cancer			
Mean	243.44	239.44	207.43
n	31.00	27.00	17.00
SD	49.25	45.62	40.71
Cancer			
Mean	224.68	223.47	215.57
n	48.00	48.00	47.00
SD	54.04	52.67	48.79
50-59			
No cancer			
Mean	187.01	172.38	162.18
n	38.00	31.00	24.00
SD	51.32	45.04	35.42
Cancer			
Mean	195.85	188.25	173.85
n	49.00	49.00	49.00
SD	44.01	48.40	46.88
60-90			
No cancer			
Mean	143.14	133.03	125.81
n	39.00	38.00	32.00
SD	42.68	36.81	33.82
Cancer			
Mean	157.61	157.57	141.74
n	27.00	27.00	26.00
SD	45.89	49.46	48.70
Total			
No cancer			
Mean	214.58	218.82	191.28
n	163.00	144.00	110.00
SD	67.94	157.43	69.77
Cancer			
Mean	211.27	210.47	199.67
n	158.00	158.00	155.00
SD	56.74	61.11	62.01

n – Number of subjects in each group; SD – Standard deviation

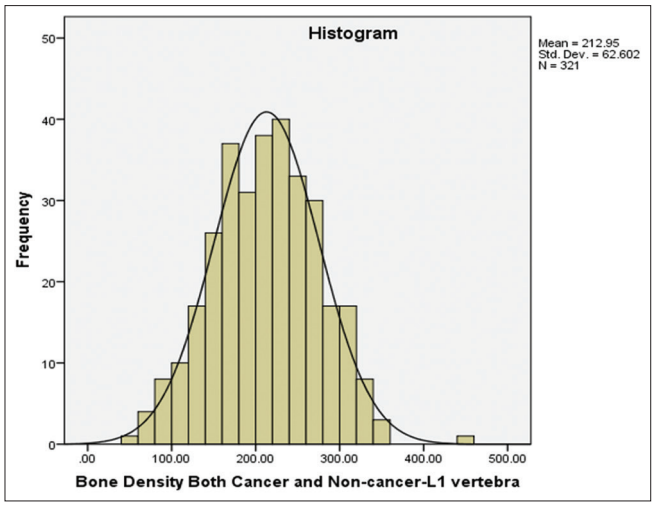

Figure 2: Histogram and Normal Distribution Curve for L1 Bone Density

correlation coefficient of − 0.52 and − 0.74, respectively, $P = 0.000$.

Based on the mean density and standard deviation as shown in Table 1 for the L1 vertebra of noncancer patients aged between 20 and 29 years, the deduced value for osteopenia (T-score between − 1 and − 2.5) was 174.4–236.4 HU and that for osteoporosis (T-score of <−2.5) was <174.4 HU.

Information on the medication used in the treatment of the patients as well as the date of diagnosis was absent or incomplete about 40% of the patients, making it difficult to evaluate the effect of chemotherapy and disease duration on bone density in our study subjects.

DISCUSSION

The mean age for the breast cancer patients was slightly higher than that of the noncancer patients, which was similar to what was found by Ramin *et al*., even though their population had more Caucasians than Blacks.[2]

The mean bone densities of the breast cancer patients in this study were generally lower than that of the noncancer patients for all the age groups which was similar to the results of other studies.[1,2] However, there was no significant difference in the overall mean bone density for cancer and noncancer patients. Bruning *et al*., Ramin *et al*., and Chen *et al*., who compared the difference in bone densities between age-matched breast cancer and nonbreast cancer cases had similar findings as this study.[1,2,12] These studies concluded after following their subjects for 5 years that the bone loss caused by the direct effect of breast cancer treatment is only during the time of their treatment. Thus, premenopausal women who were not rendered menopausal by their treatment will continue to form bone to replace lost bone until they become menopausal. They further stated that the difference may be significant in patients who develop their cancer after menopause where they cannot replace the bone loss caused by their treatment or cancer. This model was corroborated by Greep *et al*., who found a significant difference between the mean bone density of cancer and noncancer subjects.[13] This was not apparent in our study possibly because patients with CT scan evidence of advanced disease who are more likely to have severe effect of cancer on their bone metabolism were excluded in this study. In addition, these patients tend to have more toxic chemotherapy which will also directly impair bone formation.

The measured HU for both cancer and noncancer patients showed a normal distribution curve validating the use of CT attenuation numbers as an index of BMD. This fact has been supported by other studies.[4,5] Hendrickson *et al*. also noted that HU for any of the L1– L4 vertebrae could be used in assessing one's risk of osteoporosis.[5]

The study found a negative but significant correlation between bone density and patient age. There was however a better correlation in noncancer patients than the cancer patients. This could be explained by the postulated effect of breast cancer on bone density which is believed to be both direct from the breast cancer and the toxic effect of chemotherapy as well as indirect from the menopause induced by the chemotherapy.[1,2,12,13]

Using the mean bone density for noncancer patients between 20 and 29 years as the reference level and the WHO definition for osteopenia and osteoporosis, values for osteopenia (T-score between − 1 and − 2.5) was estimated to be between 174.4 and 236.4 with osteoporosis being bone density <174.4.[5] This range can be used as a reference level to screen for osteoporosis in West African breast cancer patients where DEXA machine is very scarce. Chen *et al*. and other researchers support screening for osteoporosis in breast cancer patients.[1] This can easily be achieved in the subregion using lumbar spine attenuation values measured on chest and abdominal CT scans requested for patients' follow-up management. Hendrickson *et al*. recommend that any breast cancer patient whose T-score falls below − 3 should be sent for assessment and possible treatment.[5]

The study had a few limitations which included the incomplete or nonavailability of information on the type of medication given and the date of diagnosis of the cancer for about 40% of the patients. This made it difficult to

objectively evaluate the effect of chemotherapy and disease duration on bone density in our study subjects. Again, it was difficult to match the cancer and noncancer groups for exact ages, so they were matched with their age groups as was summarized at the results section.

In conclusion, this study has been able to show that using CT attenuation values for lumbar vertebra to estimate bone density is objective and accurate. This is because the measured bone densities followed a normal distribution, the mean bone densities for breast cancer patients were generally lower than noncancer patients and there was a better correlation between patient age and lumbar vertebra bone density in noncancer patients than breast cancer patients. The study was able to determine a reference range for screening for osteoporosis in West African breast cancer patients.

It is recommended that clinicians managing breast cancer patients in resource-poor countries adopt this method of assessing bone density of their patients using follow-up CT scans to help screen for osteoporosis. The opportunistic use of CT attenuation values as an index of bone density can also be adopted to assess the risk of osteoporosis in the at-risk population which is said to be lacking in sub-Saharan Africa.[14] A larger prospective study with more breast cancer patients should be conducted to ascertain the effect of chemotherapy, extent and duration of disease on bone density.

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Conflicts of interest
There are no conflicts of interest.

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