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CT Thresholds for Spinal Bone Mineral Attenuation to Prioritize Eligible Older Women for Osteoporosis Screening

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Abstract

Introduction: Computed tomography (CT) measurements of bone mineral attenuation may be a useful means to identify older women who should be prioritized for bone mineral density screening. Methods: We compared bone mineral attenuation as measured in the L1 vertebra of CT studies to the results of dual-energy x-ray absorptiometry (DEXA) studies to determine what CT attenuation thresholds might yield a reasonable combination of sensitivity and specificity for the detection of osteoporosis. The study was limited to women between the ages of 65 and 75 years who had a DEXA study and a CT that included the L1 or adjacent vertebra performed within 3 years of the DEXA study. Results: There were 1226 women in this study, of whom 452 (38%) had osteoporosis based on a T-score ≤ −2.5 by DEXA. There were 830 CT studies performed with contrast and 396 studies which were performed without contrast. There was a statistically significant difference in the mean HU of those studies performed without contrast compared to those with contrast (unenhanced mean 103 HU versus 125 HU, $p < 0.001$). Different CT attenuation thresholds provided the most appropriate combination of sensitivity and specificity for the detection of osteoporosis when comparing CT studies performed without or with IV contrast and when all the CT data were used in aggregate. Conclusion: Different thresholds appear necessary when using the mean CT vertebral attenuation to identify older women for preferential referral for DEXA studies.

Keywords

Osteoporosis, Bone Mineral Attenuation, CT Threshold

1. Introduction

Osteoporosis, which is defined as low bone mass, is a major public health concern [1] as it leads to decreased bone strength and increased risk of low-trauma fracture [2]. There are more than 2 million fractures reported in the United States each year which are related to osteoporosis [3]. Annual cost of caring for these individuals with osteoporotic fractures is high, having been shown to exceed the costs of caring for those with breast cancer, myocardial infarction, or stroke in women ages 55 years and older [4].

Screening for high fracture risk and subsequent treatment in older women can reduce fractures related to osteoporosis [5]. Given the large impact osteoporosis has on healthcare, it is crucial to identify women with osteoporosis that have an increased fracture risk. Dual-energy x-ray absorptiometry (DEXA) of the lumbar spine and hips is currently the gold standard in diagnosing osteoporosis [6]. This technique utilizes x-rays of 2 different energies which allow the bone to be delineated from the surrounding soft tissue, thus giving an estimate bone mineral density (BMD) [7]. The number of standard deviations the BMD is relative to the mean BMD of a healthy young adult is reported via a T-score [8]. In combination with other clinical parameters, DEXA can provide a good estimate of an individual's fracture risk [7].

The United States Preventive Services Task Force (USPSTF) recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older [9]. However, there is poor compliance with these recommendations as it is estimated that more than 50% of eligible women 65 years or older have not had a DEXA study [10]. In addition, there is insufficient capacity in our integrated health care (IHS) system to image all eligible women for osteoporosis using DEXA studies. Eligible women who desire screening must often wait 3 to 6 months in order to receive non-emergent DEXA studies. Therefore, a method to prioritize women for DEXA studies would be beneficial.

Computed tomography (CT) uses an x-ray beam which is projected around the body and subsequently reconstructed to produce cross sectional or volumetric images. CT scans are widely performed for a multitude of indications which can include but are not limited to abdominal pain, infection, and trauma. Measurements of BMD of the lumbar vertebrae have been shown to correlate well with both the DEXA measurements of the lumbar spine as well as associated with increased prevalence of vertebral compression fractures [11]. There is not yet enough data to conclude that CT BMD measurements of the lumbar spine can identify all patients with osteoporosis. However, CT BMD measurements may help identify those women at higher risk for osteoporosis and who may most benefit from DEXA studies. The purpose of this study was to determine if there are specific thresholds for CT attenuation of the bone mineral density of the L1 or adjacent vertebrae, which may be optimal for patient selection to undergo subsequent DEXA studies.

2. Methods

This study was approved by the Institutional Review Board, and in keeping with the policies for a retrospective review with no direct patient interactions, informed consent was not required. We looked at all women between the ages of 65 and 75 who had a BMD study performed in 2018 or 2019 and a CT study that included at least the L1, T12, or L2 vertebra with no more than 3 years between the two studies.

Two different authors measured the mean Hounsfield units (HU) attenuation of the L1 vertebra's central matrix. If the L1 vertebra was fractured or incompletely visualized, we measured the central matrix of the T12 vertebra. If both the L1 and T12 vertebra were fractured or incompletely visualized, then the central matrix of the L2 vertebra was measured. The central bone matrix was measured in the axial plane at three contiguous slices centered at the middle of the vertebral body. The lowest mean HU attenuation of the three measurements from the axial plane was recorded. The average of the 2 lowest mean attenuation values measured by the observers was used for the primary analysis.

The patient's age was recorded, as well as the make and model of the CT scanner. Only studies performed with a KVP of 120 were utilized. The use of intravenous contrast was also recorded. If the CT study included both pre and post IV contrast-enhanced images, both sets of images were measured, but for the primary analysis, the mean attenuation of the unenhanced images was utilized.

The T-score of the patients corresponding BMD study were recorded as per the radiology report. Women with a T-score ≤ −2.5 were considered positive for osteoporosis.

Receiver operator curves (ROC) were generated by comparing the mean attenuation of the measured vertebra to the likelihood of osteoporosis based on the BMD study.

All statistical analyses were performed using online statistical software https://www.socscistatistics.com or Microsoft Excel (version 2021, Microsoft Corp, Redmond WA).

3. Results

There were 1226 women between the ages of 65 and 75 (mean age 69.3 ± 3.3 years) who underwent CT imaging and corresponding DEXA study within 3 years of each other. **Table 1** provides the breakdown in age and number with osteoporosis as defined by T-score ≤ −2.5. In this population, osteoporosis was present in almost 40% of women undergoing a DEXA study, except for those aged 65, in whom the prevalence was 28%. **Table 1** also provides the mean axial HU values for women without and with osteoporosis within each age group.

There were 830 CT studies performed with contrast and 396 studies which were performed without contrast. This latter group includes 89 studies that were performed without and with contrast, for which the attenuation of the

Table 1. All women 65 - 75 years of age and those with osteoporosis (T-score ≤ −2.5). Mean HU measurements by age. IQR = interquartile range.

age	total	Number with t ≤ −2.5 (% of total)	Mean Axial HU (IQR) all subjects	Mean Axial HU (IQR) with osteoporosis	Mean Axial HU (IQR) without osteoporosis
65	240	68 (28)	128 (43)	118 (47)	133 (47)
66	122	49 (40)	122 (41)	112 (34)	128 (49)
67	99	38 (38)	118 (41)	103 (36)	127 (36)
68	86	32 (37)	124 (46)	108 (55)	134 (35)
69	103	42 (40)	113 (52)	112 (40)	122 (45)
70	116	43 (37)	114 (44)	104 (48)	121 (39)
71	102	42 (41)	107 (43)	95 (34)	116 (37)
72	97	35 (36	112 (48)	99 (31)	121 (44)
73	87	33 (37)	110 (46)	97 (33)	119 (48)
74	79	32 (40)	112 (37)	104 (31	118 (49)
75	95	38 (40)	122 (41)	103 (31)	121 (36)
total	1226	452 (38)	117 (47)	105 (45)	125 (45)

unenhanced images was utilized in the primary analysis. There was a statistically significant difference in the mean HU of those studies performed without contrast compared to those with contrast (unenhanced mean 103 HU versus 125 HU, $p < 0.001$). For the 89 studies that included unenhanced and enhanced images, there was a statistically significant increase in mean HU on the enhanced images (unenhanced 111 HU versus 126 HU, $p < 0.001$).

The ROCs are presented in **Figures 1-3**. The AUC is 0.77 for the ROC of unenhanced CT studies. Our findings suggest that a threshold of 100 HU would provide a reasonable level of sensitivity (76.9%) and specificity (59.7%) for CT studies performed without contrast. The AUC is 0.71 for the ROC of contrast-enhanced CT studies. A threshold of 120 HU would provide a reasonable level of sensitivity (62.2%) and specificity (60.3%). The AUC is 0.70 for the ROC using comingled data from unenhanced and contrast-enhanced CT studies. If only one CT threshold is to be utilized, then an intermediate threshold value such as 110 HU would yield a sensitivity of 59.5% with a specificity of 64.1%.

There were 1134 studies for which the L1 vertebra was measured. There were 78 studies in which the T12 vertebra was measured and 14 in which the L2 vertebra was utilized. There was a statistically significant difference in the mean attenuation measured at L1 compared to T12 or L2 (L1 mean HU 119 versus T12 or L2 mean HU 102, $p < 0.001$). There were vertebral compression fractures in 54 of these 92 studies, including all 14 studies where the L2 vertebra was measured. For the remaining 38 studies, the T12 vertebra was measured because the L1 vertebra was incompletely imaged.

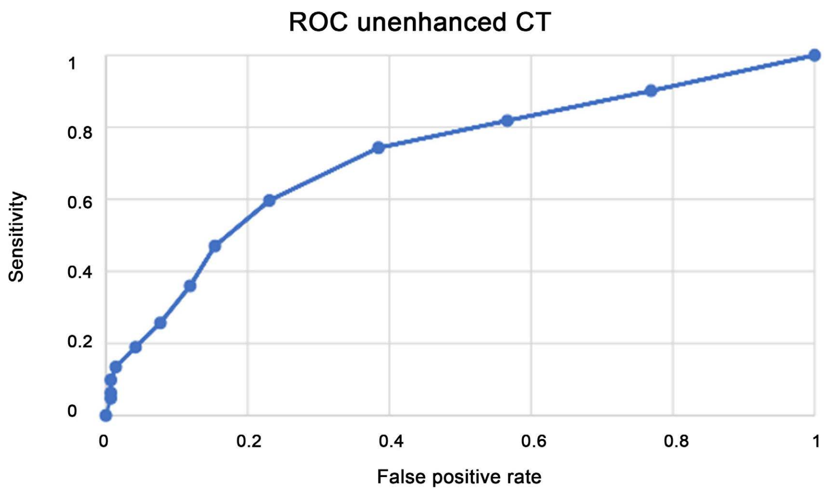

Figure 1. ROC analysis using only unenhanced studies. AUC = 0.77.

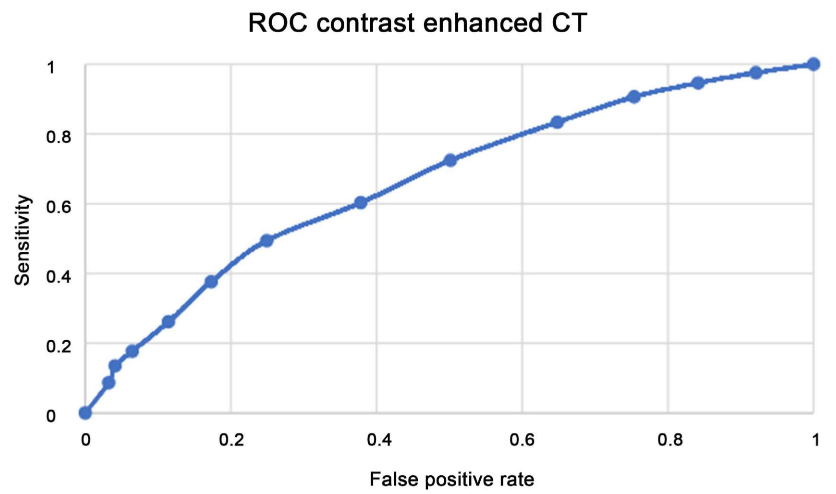

Figure 2. ROC analysis using only the contrast-enhanced studies. AUC = 0.71.

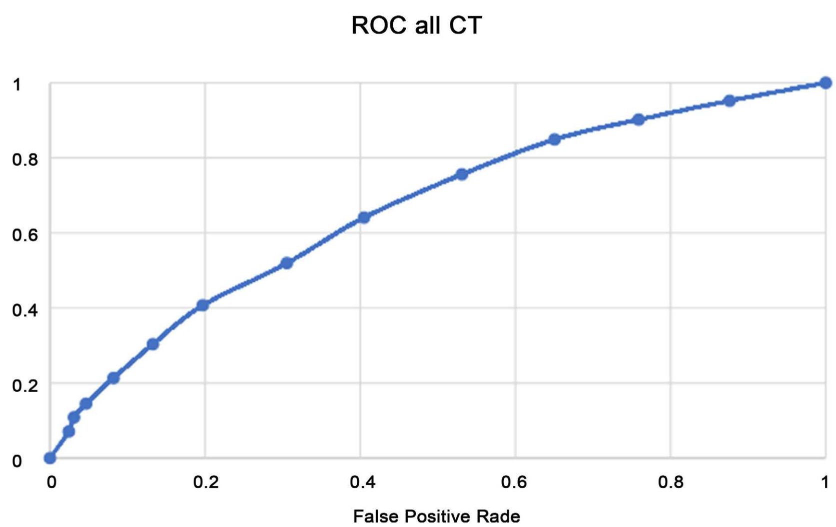

Figure 3. ROC analysis using all non-contrast and contrast-enhanced CT studies is shown in AUC = 0.70.

There were an additional 77 subjects with compression fractures identified on CT to give a total of 131 fractures of at least moderate (25% or greater compression) severity among all 1226 subjects for a prevalence of 10.7%. Of these 131 subjects, 64 (48.8%) had osteoporosis based on corresponding DEXA studies. There was a significant difference in the mean axial HU attenuation of the 131 subjects with a compression fracture versus those without fracture (91 HU versus 121 HU, $p < 0.001$).

The average absolute difference in mean HU attenuation of the vertebral central bone matrix between the two observers was 8 HU with IQR 9 HU. If we used a 100 HU threshold to identify subjects for expedited referral for a DEXA study, there would have been concordance between the two observers in 324 of the 396 subjects with unenhanced CT studies (81.8%). If we used a 120 HU threshold to identify subjects for expedited referral for a DEXA study, there would have been concordance between the two observers in 757 of the 830 subjects with contrast-enhanced CT studies (91.2%).

The median interval between the DEXA study and the CT was 238 days (Interquartile range 354 days). The minimum interval was 0 days (*i.e.*, CT and DEXA performed on the same day), with a maximum interval of 901 days.

4. Discussion

The USPSTF recommendations for routine screening for osteoporosis for women 65 years and older have been present since 2002 and most recently updated in 2018 [9]. However, the number of eligible women who undergo screening remains low with a recent study by Ruiz-Esteves *et al.*, suggesting that less than 40% of eligible white women are screened and less than 10% of eligible black women [12]. In this IHS, in which there is currently inadequate capacity to perform routine DEXA studies on all eligible women 65 years or older, a method to determine which older women might be at greatest risk for osteoporosis would help give them priority for DEXA studies.

There have been several studies on the utility of opportunistic screening for osteoporosis based on vertebral CT attenuation and their correlation to DEXA studies. A recent meta-analysis of nine such studies performed by Ahern *et al.* [11] demonstrated that all 9 studies used for the meta-analysis demonstrated a good correlation between CT and DEXA T-score, However, the CT attenuation thresholds varied between studies, possibly due to differences in the patient populations evaluated in these studies. For example, in the most extensive study of 1,867 subjects by Pickhardt *et al.* [13], the mean age of subjects was 59.2 years and included 356 men. The lower mean age and inclusion of men may account for the lower percentage of osteoporotic subjects in this group (22.9%) and the lower percentage of patients with vertebral compression fractures (6.4%). In the same study, 54.6% of CT examinations were performed with IV contrast; the authors found no significant difference between the AUCs of unenhanced and contrast-enhanced CTs. They conclude that a 135 HU threshold yielded a balanced sensitivity and specificity of approximately 75% for the DEXA diagnosis of osteoporosis [13]. Optimal thresholds have varied in multiple other studies [14]-[21] ranging from <100 HU for high specificity to >170 HU for high sensitivity. In none of these studies was the study population limited to women 65 years or older. Therefore, the results of the current study add additional insight into the most appropriate CT threshold to use to identify women for expedited DEXA screening.

Our results suggest that different thresholds may be necessary depending on whether the CT attenuation measurements of the central bone matrix of the L1 or adjacent vertebra are obtained on a contrast-enhanced or unenhanced CT.

Not unexpectedly, the only significant osteoporosis-related variables identified from logistic regression were CT attenuation and the presence or absence of IV contrast. Age was not a significant variable, likely due to the limited range of the women in this analysis.

5. Limitations

The primary limitation of this study is the time interval between the DEXA and CT studies. The median interval was 238 days, and the interquartile range was almost 1 year (354 days). However, it should be noted that previous studies have demonstrated that only patients with advanced osteopenia (T-score between −2.0 and −2.49 have up to a 10% likelihood of becoming osteoporotic within 1 - 1.5 years [22] [23]. Subjects with normal or mild/moderate osteopenia (T-score > −2.0) are unlikely to develop osteoporosis for 5 - 15 years. In this study, 309 subjects had advanced osteopenia, only 63 subjects had their CT study more than one year after their DEXA, and no one had more than a two-year interval. Therefore, the T-scores are likely a valid representation of the overall bone mineral density at the time of the corresponding CT.

Furthermore, while the DEXA study is the standard for diagnosing osteoporosis, it does not always predict major osteoporotic fractures. For example, in this study population, 131 subjects were found to have at least one moderate vertebral compression fracture in the imaging field of view. However, only 64 subjects (48.8%) had a T-score ≤ −2.5 on their corresponding DEXA study. Given the increasing evidence for the utility of several pharmacologic agents in preventing further osteoporotic fractures [24], the utilization of a clinical risk calculator such as FRAX which may include bone mineral density should always be encouraged.

We chose to include women in this study who were between the ages of 65 - 75 as we were interested in a means to identify women for expedited DEXA screening among those who were undergoing CT for unrelated reasons. Therefore, it is not surprising that in this analysis age was not a significant osteoporosis-related variable given the very limited age range in our study.

Finally, there are some factors which can affect the HU measurement on CT studies. These factors include body composition, patient weight, or artifact. Although the spine is not as vulnerable to these effects compared to the more central structures, this study did not evaluate these variables or their effect on our vertebral body HU measurements.

6. Conclusion

Different thresholds appear necessary when using the mean vertebral attenuation to identify older women for preferential referral for DEXA studies. A cutoff value of 100 HU for unenhanced CT studies and 120 HU for contrast-enhanced CT studies provides the most helpful combination of sensitivity and specificity for the detection of osteoporosis in older women between the ages of 65 and 75.

Authors' Contributions

Seo Yeon Orite participated in the data collection, data analysis, and manuscript preparation. Bryn Higuchi participated in the data collection, data analysis, and manuscript preparation. Hyo-Chun Yoon participated in the study design, data analysis, manuscript preparation and manuscript submission. Lana Gimber participated in the study design and manuscript preparation.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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