Prevalence of Vertebral Compression Fractures on Routine CT Scans According to L1 Trabecular Attenuation: Determining Relevant Thresholds for Opportunistic Osteoporosis Screening

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OBJECTIVE. Radiologists interpreting body CT scans may be the first to identify osteoporosis and associated vertebral fractures. This study correlates L1 trabecular attenuation measurements with prevalent vertebral body fractures in older adults undergoing routine CT.

MATERIALS AND METHODS. Mean L1 trabecular attenuation was measured at thoracoabdominal CT in 1966 consecutive adults (983 men and 983 women) 65 years and older (mean age, 74.1 ± 6.6 [SD] years). Sagittal reconstructions and lateral scouts were analyzed for moderate or severe thoracolumbar vertebral compression fractures according to the Genant semiquantitative assessment method. The diagnostic performance of L1 attenuation for the evaluation of prevalent vertebral fractures was assessed, including ROC curve analysis.

RESULTS. A total of 162 (8.2%) individuals (mean age, 78.3 years; 66 men, 96 women) had at least one moderate or severe vertebral fracture. The mean L1 attenuation was 70.2 HU among patients with a prevalent fracture, whereas it was 132.3 HU among patients without fracture ($p < 0.001$). The prevalence of moderate or severe vertebral compression fractures was 32.5% when L1 attenuation was ≤ 90 HU. Prevalence increased to 49.2% with L1 attenuation of ≤ 50 HU. ROC curve analysis determined an optimal threshold of 90 HU (sensitivity = 86.9%, specificity = 83.9%), with a corresponding AUC of 0.895. The odds ratio of having a moderate or severe vertebral compression fracture was 31.9 for L1 attenuation ≤ 90 HU (95% CI, 20.2–50.5; $p < 0.001$).

CONCLUSION. Patients with moderate or severe vertebral compression fractures have significantly lower L1 attenuation values than patients who do not. L1 attenuation ≤ 90 HU may represent an optimal threshold for determining risk for osteoporotic vertebral fractures.

Keywords: bone mineral density, CT, fracture, opportunistic screening, osteoporosis

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Osteoporosis is a major health problem affecting older adults, and its disease burden is one of the largest worldwide [1]. Ten million Americans have an established diagnosis of osteoporosis, 80% of whom are women [2], and 2.2 million osteoporotic fractures occur every year in the United States alone [3]. Despite the significant morbidity associated with these fractures, osteoporosis and osteopenia still remain underdiagnosed and undertreated [4]. Dual-energy x-ray absorptiometry (DEXA) screening is currently underutilized [5] with rates shown to be as low as 10–33% in various groups [6], which highlights the need for further methods to cover this care gap.

Opportunistic bone mineral density (BMD) evaluation can detect osteoporosis in patients undergoing CT for common indications [7–12]. Routine assessment of sagittal reconstructions for vertebral compression fractures and measurement of the attenuation (in Hounsfield units) of trabecular bone in the first lumbar vertebral body (L1) are examples of two approaches that can identify patients at increased fracture risk [12–14]. This opportunistic evaluation of BMD by radiologists for patients undergoing routine CT could improve screening rates at little to no extra expense, time, or radiation dose.

In particular, prevalent vertebral fractures are one of the biggest risk factors for future fragility fractures [15]; however, many vertebral fractures are missed at CT without the use of the sagittal view [13]. Radiologists interpreting thoracoabdominal CT scans may be the first to identify low BMD and associated vertebral compression fractures, which are generally sufficient for a diagnosis of osteoporosis [16]. It has previously been shown that L1 attenuation values are correlated with spinal DEXA T-scores [12, 17, 18], but it is not well established if L1 attenuation mea-

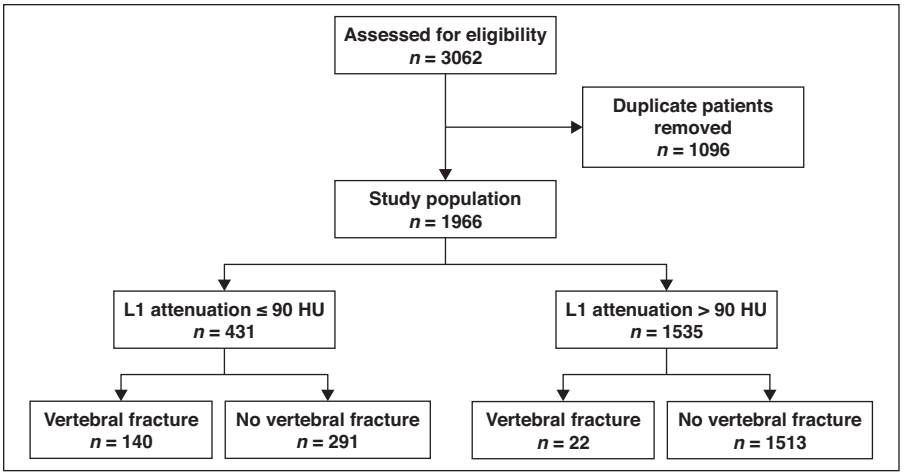

Fig. 1—Flow diagram shows patients included in study group and distribution of patients with vertebral fracture and those without vertebral fracture based on L1 attenuation.

surement is indicative of underlying vertebral compression fracture status. Thus, this study sought to characterize L1 attenuation in an older adult patient population composed of patients with and those without vertebral fractures who underwent routine body CT to determine if L1 attenuation is associated with prevalent vertebral compression fractures.

Materials and Methods

Patient Cohort

The institutional review board approved this HIPAA-compliant retrospective study. The need for obtaining signed informed consent was waived for the retrospective analysis. The initial study cohort was identified by searching the institutional PACS database for all CT examinations including the chest or abdomen performed in 2003. Any patient 65 years or older who underwent a thoracoabdominal CT ex-

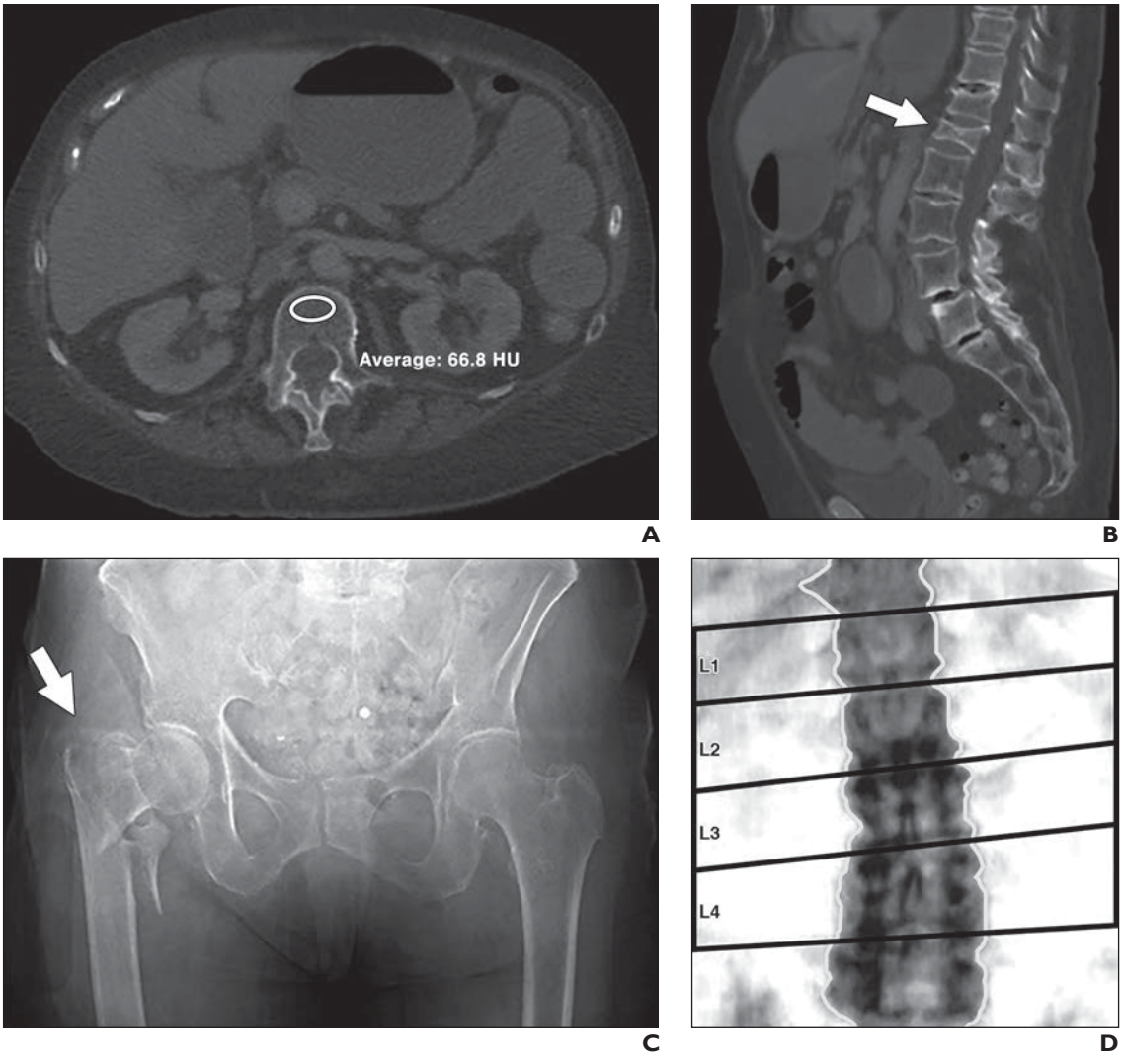

Fig. 2—Abdominal CT of 84-year-old woman. Examination was performed for evaluation of abdominal pain and discomfort. **A** and **B,** Axial (**A**) and sagittal (**B**) images. Because of severe compression fracture at L1 (*arrow*, **B**) and moderate compression at T12, ROI trabecular attenuation measurement was placed at L2 level (**A**). Trabecular attenuation is low in this case, measuring 66.8 HU. **C,** CT image obtained 6 months after **A** and **B** shows hip fracture (*arrow*). **D,** Dual-energy x-ray absorptiometry (DEXA) screening had been performed 8 years before **C**. DEXA image shows osteopenia with T-score of –1.8 at L1–L4.

TABLE 1: Patient Demographics and CT Examination Characteristics Based on Fracture Distribution

Patient	Vertebral Fracture (*n* = 162)	No Vertebral Fracture (*n* = 1804)	Total (*n* = 1966)	*p*
Age				< 0.001[a]
Mean	78.3	73.7	74.1	
SD	6.5	7.1	6.6	
Sex				0.014[b]
Male	66 (41)	917 (51)	983 (50)	
Female	96 (59)	887 (49)	983 (50)	
Study type				0.214[b]
Chest only	29 (18)	442 (25)	471 (24)	
Chest and abdomen	19 (12)	142 (8)	161 (8)	
Chest, abdomen, and pelvis	26 (16)	277 (15)	303 (15)	
Abdomen only	17 (10)	163 (9)	180 (9)	
Abdomen and pelvis	71 (44)	780 (43)	851 (43)	
Use of contrast material				0.743[b]
Contrast-enhanced study	99 (61)	1126 (62)	1225 (62)	
Unenhanced study	63 (39)	678 (38)	741 (38)	

Note—Unless indicated otherwise, data are number (%) of patients.
[a]Mann-Whitney *U* test.
[b]Chi-square test.

amination during that period that showed L1 was included in the study. Exclusion criteria were a CT study that did not show the entire L1, image artifact that obscured the spine, or the presence of any hardware or metal associated with the spine. If a patient underwent multiple examinations during the study period, only their first examination was used for analysis. The final cohort consisted of 1966 patients, ranging in age from 65 to 95 years old (983 men, 983 women; mean age, 74.1 ± 6.6 [SD] years). Figure 1 illustrates the flow diagram of patient inclusion and distribution of fractures.

CT Acquisition

All CT examinations were performed on a variety of MDCT scanners using a 120-kVp setting and variable tube current. Examinations included images obtained without contrast material and those obtained after administration of oral or IV contrast material, as would typically be encountered in daily practice. Rigorous daily water phantom quality assurance checks, as suggested by the American College of Radiology, are performed at both isocenter and off isocenter on all scanners throughout the institution to ensure precision and stability.

Image Analysis

Each CT examination included the L1 trabecular space as well as the thoracic spine, lumbar spine, or both depending on anatomic coverage. Vertebral assessment at CT was performed on a standard PACS workstation; images were viewed in a typical bone window setting (width, 1200 HU; level, 350 HU). A single ovoid 100–300 mm ROI for measuring mean attenuation values (in Hounsfield units) was placed within the L1 trabecular bone on the transverse (axial) series (Fig. 2). Care was taken to avoid the posterior venous plexus, focal heterogeneity, or any imaging-related artifacts. This simple ROI attenuation method does not require a phantom, oblique angulation along the disk plane, multilevel assessment, or ROI placement in muscle and fat, which may be performed in quantitative CT [12].

The L1 vertebral level was primarily used given that this level is easily identified at CT as the first non–rib-bearing vertebra, is included on all abdominal and thoracic CT scans in clinical practice, and provides the best overall results in terms of DEXA correlation [12]. If the measurement in L1 was altered because of a compression fracture or impaired quality of the reconstruction, an identical measurement was taken at an adjacent vertebra amenable to measurement (Fig. 2). BMD measurements and fracture assessments were initially performed by one student coauthor trained by radiologist coauthors and subsequent confirmation was performed by a board-certified radiologist with 10 years of clinical experience. Fracture assessment was performed according to the Genant semiquantitative scale [19], which was originally intended for conventional radiography but is adaptable to sagittal CT reformations as well. This simple 4-point scale classifies vertebral bodies as normal (grade 0) or as having a mild (grade 1), moderate (grade 2), or severe (grade 3) deformity. Only grade 2 (moderate) or grade 3 (severe) compression fractures were recorded to ensure that an anatomic variation was not misrepresented as a fracture and that subtle mild fractures (vs normal) were excluded.

The variables recorded in the retrospective analysis included: age, sex, study date, study type, use of contrast material, average L1 trabecular attenuation, presence of fracture, fracture level, and fracture grade based on the Genant semiquantitative scale.

Statistical Analysis

Continuous variables are summarized with mean and SD values; categoric measures are summarized with frequency counts and percentages. Chi-square or Mann-Whitney *U* tests were used to assess differences between groups in continuous and categoric variables. An ROC curve analysis was used with an AUC calculated for attenuation thresholds according to fracture prevalence. Odds ratios and 95% CIs were obtained; $p < 0.05$ (two-sided) was the criterion for statistical significance. All statistical analyses were performed using R software (version 3.1.0, The R Foundation).

Results

A total of 162 (8.2%) individuals (mean age, 78.3 years; 66 men, 96 women) had at least one moderate or severe vertebral fracture; there were 216 vertebral fractures total (Table 1). Forty-three (26.5%) patients in the fracture cohort had more than one fracture, with 11 (6.8%) patients having two or more fractures. Patients with vertebral fractures were more likely to be female and were older than those without fractures (Table 1). The mean L1 attenuation was significantly lower among patients with a vertebral fracture (70.2 HU) compared with those without a vertebral fracture (132.3 HU) ($p < 0.001$) (Fig. 3). Age had a moderately negative correlation with L1 attenuation in patients without a fracture ($r = –0.22$, Fig. 4). However, age had almost no correlation with mean L1 attenuation in patients with a vertebral fracture ($r = –0.08$).

The vertebral fracture prevalence progressively increased as the L1 threshold was lowered (Table 2). Moderate or severe vertebral fractures were present in 32.5% of patients with an L1 attenuation value ≤ 90 HU. This prevalence increased to 49.2% in patients with an L1 attenuation ≤ 50 HU. The odds ratio for having a moderate or severe vertebral compression fracture was 31.9 when L1 attenuation was ≤ 90 HU (95% CI, 20.2–50.5; $p < 0.001$). Likewise,

TABLE 2: Characteristics of Different Attenuation Thresholds for Predicting Vertebral Fractures

L1 Attenuation Threshold	Sensitivity (%)	Specificity (%)	Prevalence (%)	PPV (%)	NPV (%)
≤ 50 HU	20.0	98.2	49.2	91.5	55.9
≤ 70 HU	53.7	93.7	42.8	86.4	73.0
≤ 90 HU[a]	86.9	83.9	32.5	72.2	93.0
≤ 100 HU	89.4	76.4	25.1	55.9	95.6
≤ 110 HU	92.5	66.9	19.8	40.8	97.3
≤ 120 HU	95.0	55.6	16.0	29.0	98.3

Note—PPV = positive predictive value, NPV = negative predictive value.
[a]Optimal threshold based on ROC curve.

the positive predictive value of a fracture at the 50-HU threshold was 91.5%. The negative predictive value of a threshold of > 110 HU was 97.3%. ROC curve analysis determined an optimal threshold of 90 HU (sensitivity = 86.9%, specificity = 83.9%), with a corresponding AUC of 0.895 (Fig. 5).

The percentage of patients with two or more vertebral compression fractures was highest in those with an L1 attenuation value of ≤ 50 HU (Fig. 6). Fractures at the T12 level were the most common, accounting for 22.7% of all fractures, followed by the L1 (16.7%) and L2 (11.6%) levels, with every other thoracic and lumbar level at 10% or less.

Discussion

Previous studies have shown that CT attenuation can be used to identify patients with low BMD [7, 12], although no known previous study has specifically evaluated the correlation between CT attenuation and prevalent fractures. This study has shown that L1 trabecular attenuation measurements are highly correlated with prevalent vertebral body fractures in older adults undergoing routine CT. Therefore, in conjunction with the results from the aforementioned studies, trabecular attenuation at routine body CT not only is an effective method for measuring BMD to assess for osteoporosis, but also it correlates well with prevalent vertebral fractures. It allows an accurate, noninvasive BMD assessment while patients undergo routine thoracoabdominal CT and requires a minimal change to clinical standard practice. By assessing trabecular attenuation, interpreting physicians can bridge the gap between patients who adhere to osteoporosis screening and those who do not.

Fractures represent complicated osteoporosis, and the biggest risk factor for a future fracture is a prevalent fracture [15]. This study showed a high sensitivity and specificity for identifying vertebral fractures at the ≤ 90 HU level and illuminated that the prevalence increases as trabecular attenuation measurements decreases. Patients at ≤ 90 HU with a prevalent fracture could be at an increased risk of incidental fractures in the future, because they were 32 times more likely to have a prevalent fracture than those with trabecular attenuation greater than 90 HU.

The findings of this study also suggest that age is significantly correlated to fracture risk and that a low attenuation value increases the risk of multiple fractures. Patients with a frac-

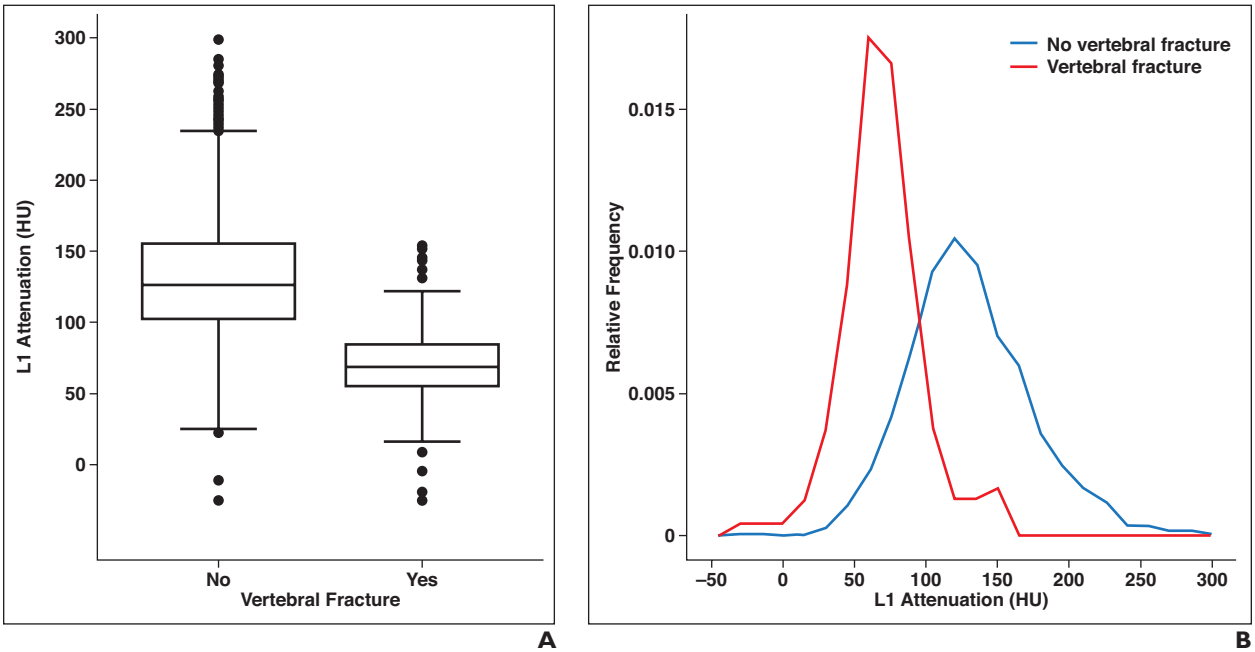

Fig. 3—L1 attenuation values in patients with and those without prevalent vertebral compression fracture.
A, Box-and-whisker plot shows distribution of L1 attenuation values in patients with and those without prevalent vertebral compression fractures. Middle lines in boxes show median HU, upper lines of boxes show third quartile limit, lower lines of boxes show first quartile limit, and whiskers show range (excluding outliers). ● = outliers.
B, Relative frequency polygon shows distribution of L1 attenuation values in patients with and those without prevalent vertebral compression fractures.

ture were approximately 5 years older on average than those without a fracture, which held true regardless of sex. The mean attenuation among the fracture cohort was approximately 60 HU lower than the mean attenuation of the nonfracture group, and 32% of patients with an attenuation ≤ 50 HU suffered multiple fractures. Because the presence of multiple fractures is one of the largest determinants of a future fracture [20], the incentive to identify patients early in the disease process is high given that treatment can decrease the risk of a future fracture, such as a catastrophic hip fracture (Fig. 2).

Increasing access to osteoporosis screening is essential for clinical practice as well as public health. Adherence rates to screening can range between 12% and 56% among various groups, including 19–97% among physicians [21–23]. By adding a supplemental method of screening to routine body CT, radiologists can identify at-risk individuals who would benefit from a DEXA examination that would guide diagnosis and be used to monitor treatment. This study suggests that CT can fill this gap: the distribution of osteoporosis and prevalent fractures in the study population is relatively like those found in other CT and DEXA studies [18, 24–26]. With this knowledge, clinicians will be able to more quickly and effectively diagnose established osteoporosis or early osteoporosis during its long preclinical phase. This study did not evaluate the probability of an incidental fracture occurring after being diagnosed with a prevalent vertebral fracture (Fig. 2), but that analysis will be performed in future work.

BMD measurements and prevalent fracture analysis could become a standard aspect of thoracic and abdominal CT to identify potential osteoporosis patients before DEXA screening. This study shows the clear segregation of L1 attenuation measurements between the fracture and nonfracture cohorts and the influence of age. Furthermore, a DEXA-equivalent femoral neck T-score can be derived from routine CT scans that include the pelvis [27, 28]. Severe lifestyle changes result after a femoral neck fracture, increasing mortality by 24% within the first year [29]. Many treatments are available if osteoporosis is diagnosed early [30–32], so these fractures are preventable and the treatment could prolong and save lives.

There are several limitations to this study, including the retrospective nature of the analysis and a lack of imaging technique standardization. A retrospective cohort study

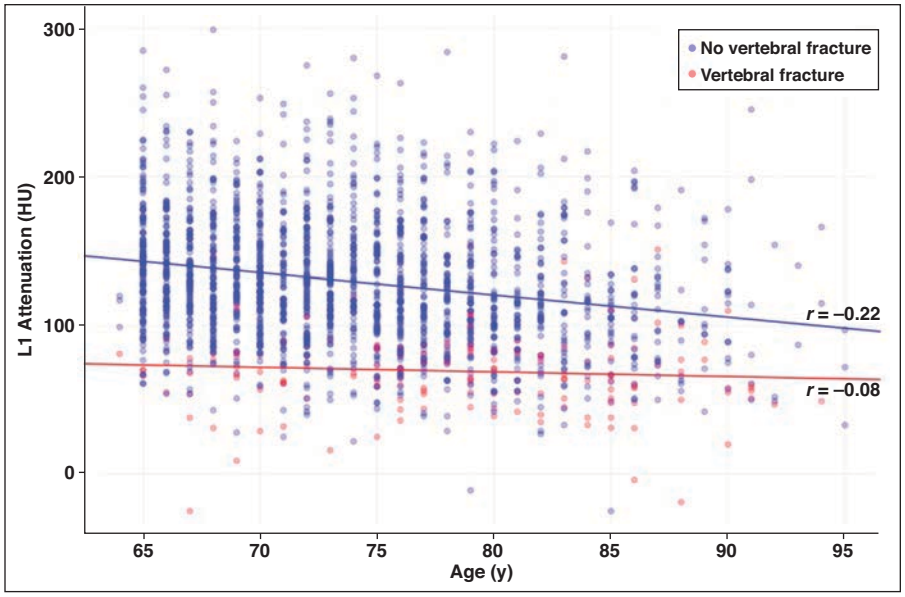

Fig. 4—Plot of age of patients with and those without vertebral fractures and L1 attenuation. Lines show correlation between L1 HU attenuation and age for each group. Blue = cohort without fracture. Red = cohort with fracture. Note how L1 attenuation decreases with age among those without fracture but remains more constant among those with fracture.

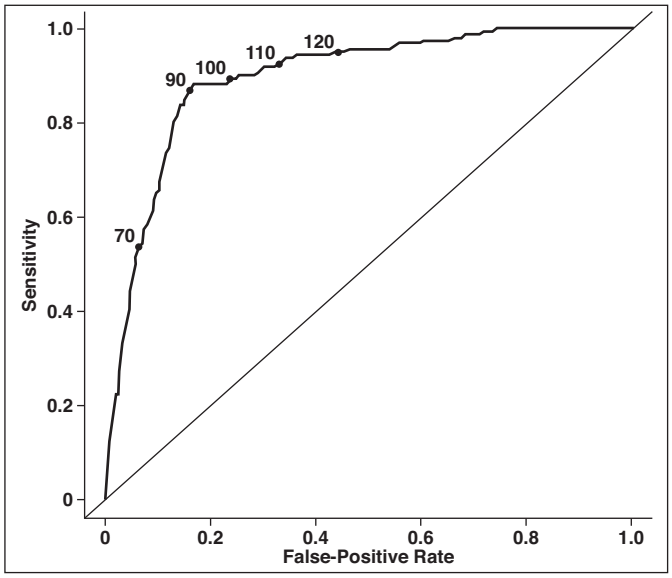

Fig. 5—ROC curve analysis of various attenuation thresholds, shown as points on ROC curve, for capturing prevalent fractures. Diagonal line is line of no discrimination, which references proximity to random association.

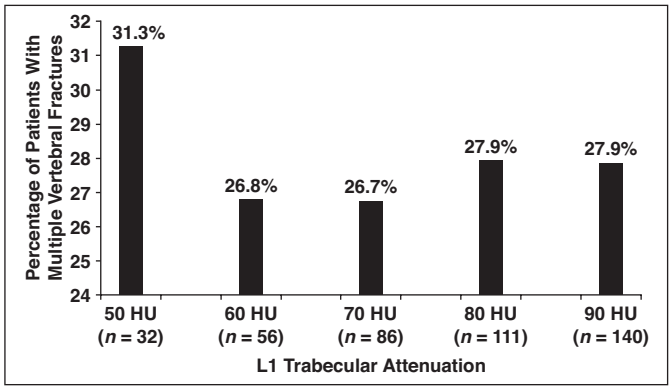

Fig. 6—Bar graph shows L1 trabecular attenuation threshold of patients who had multiple vertebral fractures.

may include unanticipated bias compared with a prospective trial, but such a large prospective trial would be expensive and impractical. Nevertheless, the patient cohort in this study was sufficiently large to hold statistical power for many of the collected variables. Another possible limitation is the lack of evaluation of the entire spine in some patients, which may have artificially lowered the number of prevalent fractures. However, the mix of examinations mirrors that in routine clinical practice. The relatively poor image quality of some sagittal scouts and reconstructions was another limitation, which again may have caused underreporting of prevalent fractures. Finally, correlation of the CT results with any prior spinal DEXA was not performed, which was thought to be beyond the scope of this study but a topic worthy of future investigation.

In conclusion, this study shows that L1 trabecular attenuation measurements are directly correlated with prevalent vertebral body fractures in older adults undergoing routine CT. Patients with moderate or severe vertebral compression fractures have significantly lower L1 attenuation values than patients who do not, and L1 attenuation ≤ 90 HU appears to represent an optimal threshold for determining risk for osteoporotic vertebral fractures. Furthermore, fracture assessment and BMD measurement at opportunistic CT produced consistently reliable results that can easily be adopted into standard practice for the detection of osteoporosis at an earlier stage. How these results can be used to predict future fracture risk remains an area for further study.

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