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ORIGINAL RESEARCH

Assessing Thoracic Vertebral Bone Mineral Density (T8-T10) for Osteoporosis Diagnosis During CT Lung Cancer Screening in Older Adults

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Introduction: Osteoporosis diagnosis often utilizes quantitative computed tomography (QCT). This study explored the validity of applying lumbar bone mineral density (LBMD) standards to thoracic vertebrae (T8-T10) for osteoporosis detection during CT lung cancer screenings. This study investigated the utility of thoracic BMD (BMD-T8-T10) for detecting osteoporosis in older persons during CT lung cancer screening.

Methods: We studied 701 participants who underwent QCT scans for both LBMD and BMD-T8-T10. Osteoporosis was diagnosed using ACR criteria based on LBMD. We determined BMD-T8-T10 thresholds via a receiver operating characteristic (ROC) curve and translated BMD-T8+T9+T10 to LBMD (TTBMD) using linear regression. Kappa test was used to evaluate the accuracy of BMD-T8-T10 thresholds and TTBMD in diagnosing osteoporosis.

Results: Raw BMD-T8-T10 poorly identified osteoporosis (kappa = 0.51). ROC curve analysis identified BMD-T8-T10 thresholds for osteopenia (138 mg/cm3) and osteoporosis (97 mg/cm3) with areas under the curve of 0.97 and 0.99, respectively. We normalized BMD-T8-T10 to TTBMD based on the formula: TTBMD = 0.9 × BMD-T8-T10 - 2.56. These thresholds (kappa = 0.74) and TTBMD performed well in detecting osteoporosis/osteopenia (kappa = 0.74).

Conclusion: Both calculating BMD-T8-T10 threshold (138.0 mg/cm³ for osteopenia and 97 mg/cm³ for osteoporosis) and normalizing BMD-T8-T10 to LBMD demonstrated good performance in identifying osteoporosis in older adults during CT lung cancer screening.

Keywords: quantitative computed tomography, thoracic vertebral bone mineral density, osteoporosis, Computed tomography, lung cancer

Introduction

Osteoporosis diagnosis often utilizes quantitative computed tomography (QCT). The diagnostic criteria for lumbar spine QCT were based on the American College of Radiology (ACR) recommendations:[1] normal, >120 mg/cm³; low bone mass, 80–120 mg/cm³; and osteoporosis < 80 mg/cm³. These thresholds have been adopted for thoracic bone mineral density (BMD) to define low or very low bone mass.[2] However, it has been shown that the thoracic BMD is usually greater than those of the lumbar spine.[3] It is necessary to evaluate whether the thresholds of lumbar spine BMD (LBMD) and the ACR criteria could be applied to the thoracic BMD.

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Chest CT scans are recommended for early lung cancer screening and coronary cardiac disease detection, which can reduce lung cancer and cardiovascular mortality rates. The target population for those detection have overlaps with the high-risk group for osteoporosis. QCT combined with routine clinical chest CT to quantify BMD enables opportunistic screening for osteoporosis without additional increase in the radiation dose or scan time. It would be interesting and helpful to evaluate osteoporosis during chest CT scans.

During a chest CT scan, the lumbar spine 1–2 (L1-2) is also imaged in approximately 11.57% of patients.[4] As a result, a few studies have demonstrated that osteoporosis can be opportunistically detected during chest CT scans.[5,6] It is challenging to determine whether people have osteoporosis if a chest scan scans only the L1 region or no region of the lumbar spine. Osteoporosis can not be evaluated based only on BMD-L1. Finding methods to assess osteoporosis using thoracic BMD would be helpful. Interestingly, few studies have showed the role of thoracic BMD in osteoporosis diagnosis.[7,8] Budoff et al[7] converted the BMD-T7+T8+T9 into equivalent LBMD, and then they obtained the T score. Their results showed that the average T-score calculated from measured lumbar spine was similar to the average T-score obtained from translated LBMD. However, their study only calculated the T-score and the performance of the ACR criteria (80 mg/cm^3) was not tested in the translated LBMD. In addition, linear regression analysis was used in a recent study to determine the cut-off points of cervicothoracic BMD for osteoporosis and osteopenia.[8] However, subjects who underwent contrast-enhanced CT scans were included, and they only showed the cut-off point of single vertebra BMD (C2-T12) for osteoporosis/osteopenia evaluation. Usually, the diagnosis is based on the average BMD of at least two vertebrae. Moreover, that study only evaluated thresholds, and the ability of the thoracic BMD to identify osteoporosis was not tested. Furthermore, the proposed thresholds were calculated by substituting 120 mg/cm^3 and 80 mg/cm^3 into the linear regression equation. It is also valuable to use other methods to determine thresholds and test their performance.

Our previous study had reported two methods for osteoporosis/osteopenia evaluation based on thoracic BMD of T11 and T12.[9] However, for some chest CT scans, such as cardiac CT examination, T11 or T12 could not be scanned. Osteoporosis/osteopenia could not be evaluated during such chest CT scan. Therefore, in this study, we aimed to show the ability of BMD-T8-T10 in diagnosing osteoporosis/osteopenia in older adults who underwent both CT scans for lung cancer screening and QCT. We adopted two methods, one is to calculate the thresholds and another is to translate TBMD to LBMD, to improve the performance of BMD-T8-T10 in diagnosing osteoporosis/osteopenia. Our study may provide more widely applicable methods for osteoporosis evaluation during chest CT scans.

Methods
Participants
The participants' information was reported in our previous study.[9] This study had the same ethics reference as the previous work as it is part of the research project. Briefly, this retrospective study was approved by the Institutional Review Board of the Affiliated Hospital of Nanjing University of Chinese Medicine (2019NL-158-01). Informed consent was waived by Institutional Review Board of the Affiliated Hospital of Nanjing University of Chinese Medicine because of the retrospective design. All patient data were anonymized. Subjects who underwent both CT lung cancer screening and QCT examinations between 2021 and 2023 were identified at our institution. Subjects whose thoracic spine (T8, T9, T10. BMD-T8-T10) and lumbar spine (L1-L2, BMD-L1+L2) were both scanned were included for further analysis. In addition, subjects with an osteoporotic compression fracture in T8-L2, history of surgery, history of tumors, ankylosing spondylitis and chronic diseases affecting bone metabolism, and who were taking drugs affecting bone metabolism were excluded. Finally, a total of 701 subjects (318 women and 383 men, 50–89 years old) were identified.

Bone Mineral Density Measurements
BMD was determined based on CT images obtained from OptimaCT660 scanner (GE, USA). The scan protocol was described in our previous study.[9] The brief scan protocol was as follows: tube voltage, 120 Kv; automatic mAs; and thickness, 0.625 mm. The CT images were transferred to the QCT workstation. Volumetric BMD measurements of the BMD-T8+T9+T10 and LBMD were performed by using commercially available software (Mindways QCT Pro;

Mindways Software, synchronous calibration). The mean BMD-T8-T10 and LBMD were calculated for osteoporosis/osteopenia evaluation. Osteoporosis/osteopenia was diagnosed based on the LBMD according to the ACR criteria.

Methods for Evaluating Osteoporosis Based on BMD-T8-T10

Three methods were used to evaluate osteoporosis based on BMD-T8+T9+T10. The first was to define osteoporosis/osteopenia using BMD-T8-T10 based on the ACR criteria (normal, >120 mg/cm^3; low bone mass, 80–120 mg/cm^3; and osteoporosis < 80 mg/cm^3). Second, we obtained new thresholds of BMD-T8+T9+T10 to define osteoporosis/osteopenia by using receiver operating characteristic (ROC) curve. Third, we obtained the linear regression equation between TBMD and LBMD, and translated TBMD to LBMD and then defined osteopenia or osteoporosis according to the ACR criteria.

Statistical Analysis

Statistical analyses were performed using the commercial software SPSS 25.0 and MedCalc (version 22.026). Comparisons between BMD-T8-T10 and LBMD were performed by using paired two-tailed t tests. The proportions of subjects with osteoporosis/osteopenia defined by the different methods were compared by Chi-square tests. The correlation between BMD-T8-T10 and LBMD was analyzed using Pearson's correlation and linear regression analysis. A receiving operator characteristic (ROC) curve was used to determine the threshold of BMD-T8+T9+T10 (Youden index) for defining osteopenia or osteoporosis. The agreement of different approaches in defining osteopenia or osteoporosis was evaluated by using the kappa test. A Bland–Altman plot was used to show the agreement between LBMD and TTBMD. Statistical significance was defined as $p < 0.05$.

Results

Characteristics of the Participants

The characteristics of the participants are shown in Table 1. The mean age was 65.0 years (women, 63.0; men, 67.2). The average LBMD was lower than that of BMD-T8-T10 (mean difference = 19.2 mg/cm^3, 95% confidence interval (CI) = −18.6 to −21.0, p < 0.01) (Figure 1A). The BMDs of T8, T9, T10 and the lumbar spine (L1-L2) were 113.3 ± 39.7 mg/cm^3, 116.8 ± 41.3 mg/cm^3, 117.3 ± 41.1 mg/cm^3 and 96.7 ± 36.3 mg/cm^3, respectively. No significant differences were observed among BMDs of T8, T9, T10 (p > 0.05). The BMDs of men were greater than those in women (p < 0.05).

The Diagnostic Performance of BMD-T8-T10 for Osteoporosis/Osteopenia Based on the ACR Criteria

The agreement of osteoporosis/osteopenia identification between BMD-T8+T9+T10 and LBMD was moderate (kappa = 0.51, 95% CI: 0.45–0.56, p < 0.001) according to the ACR diagnostic criteria (Figure 1B). The positive predictive value (PPV) and specificity were high (> 98%), but the negative predictive value (NPV) and sensitivity were low (Table 2). Only 57.6% (156/271) and 52.9% (129/244) of the subjects were diagnosed with osteoporosis/osteopenia, respectively,

Table 1 Characteristics of the Subjects

	Overall Population (n = 701)	Women (n = 383)	Men (n = 318)
Age (years)	65.5 ± 12.5	63.0 ± 11.9	67.2 ± 12.6
Postmenopause (yes)	N/A	362	N/A
BMI (kg/m^2)	23.24 ± 2.77	22.4 ± 2.86	24.03 ± 2.63
BMD-L1+L2 (mg/cm^3)	96.7 ± 36.3	88.6 ± 33.7	102.4 ± 37.4
BMD-T8 (mg/cm^3)	113.3 ± 39.7	106.0 ± 42.5	119.5 ± 36.1
BMD-T9 (mg/cm^3)	116.8 ± 41.3	111.7 ± 44.5	121.3 ± 37.9
BMD-T10 (mg/cm^3)	117.3 ± 41.1	112.3 ± 43.5	121.6 ± 38.6
BMD-T8+T9+T10 (mg/cm^3)*	115.9 ± 39.8	105.3 ± 38.7	122.5 ± 40.6

Note: *p < 0.05, vs BMD-L1+L2 both in men and women.
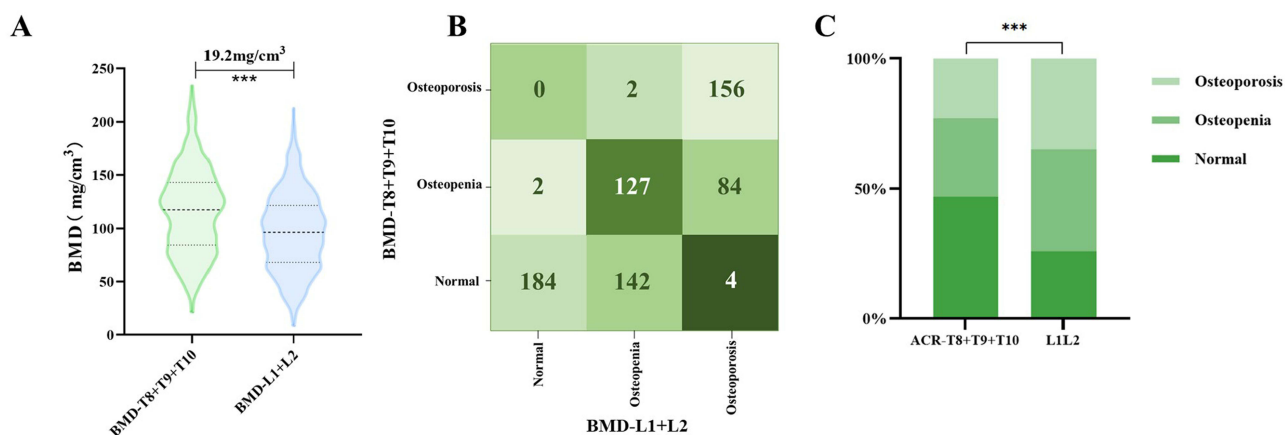**Abbreviations**: BMD, bone mineral density; BMI, Body mass index.

Figure 1 Role of thoracic vertebral bone mineral density (BMD-T8+T9+T10) in identifying osteopenia and osteoporosis based on one American College of Radiology (ACR) criterion. The difference between thoracic vertebral bone mineral density (BMD-T8-T10) and lumbar bone mineral density (LBMD) (**A**) The kappa test showed moderate agreement in identifying osteoporosis between BMD-T8-T10 and lumbar spine BMD (kappa = 0.51) (**B**). Compared to those in the gold standard group, the proportions of osteopenia and osteoporosis defined by BMD-T8+T9+T10 groups were significantly different (**C**) ***, P < 0.001.

when the 80 mg/cm^3 threshold was used for BMD-T8+T9+T10, which was significantly lower than the gold standard (p < 0.01) (Figure 1C).

Calculating the Cut-off Point of Thoracic Vertebral Bone Mineral Density

Subsequently, we calculated the cut-off point of BMD-T8-T10 for diagnosing osteoporosis/osteopenia using ROC curves. 138.0 mg/cm^3 had acceptable performance in identifying osteopenia (area under the curve (AUC) = 0.98, with a sensitivity of 86.0%, specificity of 83.4%) (Figure 2A) and 97.0 mg/cm^3 had good performance in identifying osteoporosis (AUC = 0.96, with a sensitivity of 90.9%, specificity of 94.5%) (Figure 2B). Then, we defined osteoporosis/osteopenia based on the two obtained thresholds of BMD-T8-T10. The agreement between BMD-T8-T10 and the gold standard for identifying osteopenia and osteoporosis was moderate (kappa = 0.74, 95% CI: 0.70–0.78, p < 0.001) (Figure 2C). The proportion of subjects with osteoporosis/osteopenia defined by the two thresholds was not significantly different compared to the gold standard (p > 0.05) (Figure 2D). The accuracy of BMD-T8-T10 was 87.1% (162/186), 72.7% (197/271) and 91.0% (222/244) for identifying normal, osteopenia, and osteoporosis, respectively. The NPV and sensitivity were greater than those defined according to the thresholds of 120 mg/cm^3 and 80 mg/cm^3 (Table 2).

Translated Thoracic Vertebral Bone Mineral Density

We found that LBMD was highly correlated with BMD-T8-T10 (r = 0.94) (Figure 3A). Therefore, we normalized BMD-T8-T10 to LBMD based on the following formula: TTBMD = 0.9 × BMD-T8-T10 - 2.56. Then, we obtained the translated BMD (TTBMD) based on the BMD-T8+T9+T10 data. The Bland–Altman plot showed good agreement between LBMD and TTBMD (Figure 3B). Subsequently, we defined osteoporosis/osteopenia based on the TTBMD according to the ACR criteria. The agreement between LBMD and TTBMD for identifying osteopenia and osteoporosis

Table 2 Performance of Low Thoracic Vertebral Bone Mineral Density (BMD-T8+T9+T10)

	Osteoporosis					Osteopenia				
	Accuracy	**PPV**	**NPV**	**Se**	**Sp**	**Accuracy**	**PPV**	**NPV**	**Se**	**Sp**
BMDa	87.2%	63.9%	99.6%	98.7%	83.4%	77.5%	46.9%	98.9%	98.4%	56.1%
BMDb	96.0%	100%	93.9%	89.7%	100%	87.4%	81.1%	86.2%	88.3%	77.6%
TTBMD	93.5%	90.1%	95.0%	90.6%	95.2%	88.4%	87.1%	78.5%	84.3%	82.0%

Notes: a based on the thresholds of 120 mg/cm^3 and 80 mg/cm^3. b based on the thresholds of 138 mg/cm^3 and 97 mg/cm^3.
Abbreviations: PPV, positive prediction value; NPV, negative positive value; Se, sensitivity; Sp, specificity.
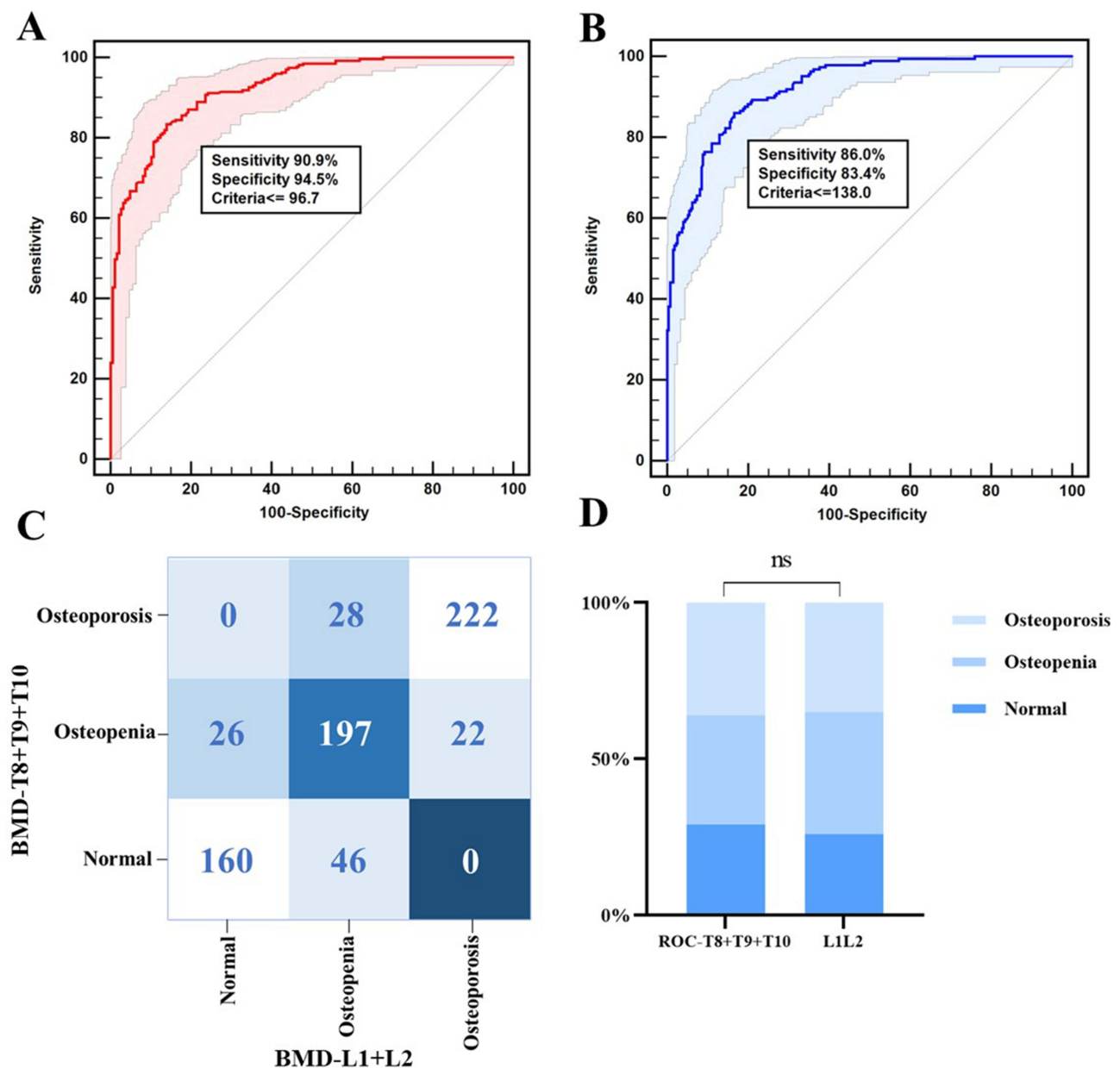
Figure 2 The performance of the thoracic vertebral bone mineral density (BMD-T8+T9+T10) in identifying osteopenia and osteoporosis. Receiver operating characteristic curves (ROC) were generated for the identification of osteopenia (**A**) and osteoporosis (**B**). The thresholds were 138 mg/cm^3 and 97 mg/cm^3. Then, we identified osteopenia and osteoporosis using these two thresholds. The kappa test showed good agreement in identifying osteoporosis between BMD-T8+T9+T10 and lumbar spine BMD (kappa = 0.74) (**C**). Compared to those of the gold standard group, the proportions of osteopenia and osteoporosis defined by the two thresholds were not significantly different (p > 0.05) (**D**). NS: not significant.

was high (kappa = 0.74, 95% CI: 0.71–0.76, p < 0.001) (Figure 3C). Compared to the gold standard, the proportion of subjects with osteoporosis/osteopenia defined by TTBMD was not significantly different (p > 0.05) (Figure 3D). The accuracy of TTBMD were 78.5% (146/186), 80.0% (216/271) and 90.1% (221/244) for identifying normal vertebrae, osteopenia, and osteoporosis, respectively. The NPV and sensitivity were greater than those defined according to the thresholds of 120 mg/cm^3 and 80 mg/cm^3, respectively (Table 2).

Discussion

During chest CT, the thoracic spine is typically examined, providing the chance to quantify the spine's BMD. The ACR suggested criteria, however, are predicated on LBMD. It is unclear what TBMD levels are for diagnosing osteoporosis.
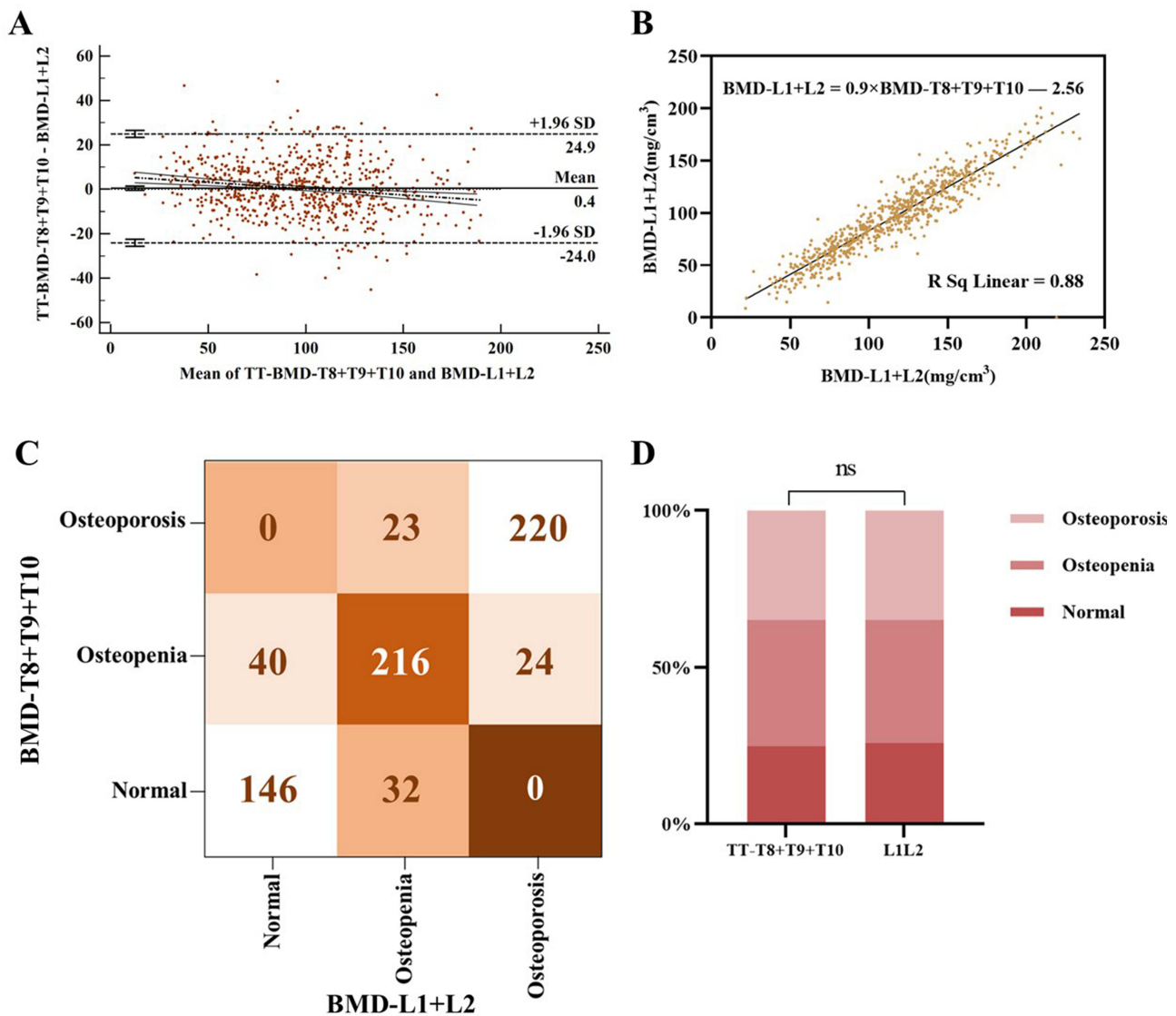
Figure 3 The Bland–Altman plot also showed good agreement between lumbar bone mineral density (LBMD) and translated thoracic BMD (TTBMD) (**A**) A formula (LBMD = 0.9 × BMD-T8-T10 – 2.56) was obtained to translate the LBMD based on the thoracic BMD (BMD-T8-T10) (**B**) and the performance of the translated LBMD in identifying osteopenia and osteoporosis was evaluated. The kappa test showed good agreement in identifying osteoporosis between the TTBMD and LBMD (kappa = 0.74) (**C**) Compared to those of the gold standard group, the the proportions of osteopenia and osteoporosis defined by TTBMD were not significantly different (p > 0.05) (**D**) NS: not significant.

The BMD of T8-T10 is usually greater than that of LBMD.[3,7,10] In addition, BMD-T8-T10 was strongly correlated with LBMD (r > 0.80).[7,11] Similar high correlation (r = 0.94) was also observed in the present study. It is possible to normalize BMD-T8-T10 to LBMD for the definition of osteoporosis due to the strong positive association. In this work, we investigated two methods for defining osteoporosis or low bone mass based on BMD-T8-T10. One is to determine whether osteopenia or osteoporosis is present by calculating the BMD-T8-T10 threshold (138.0 mg/cm^3 for osteopenia and 97 mg/cm^3 for osteoporosis). The alternative is to normalize the BMD-T8-T10 data to LBMD and then classify osteopenia or osteoporosis according to the ACR criteria. Both approaches demonstrated strong agreement with the LBMD-based strategy. Our study identified tools for diagnosing osteoporosis if the BMD of L1 and L2 cannot be assessed via chest CT.

Several studies have shown that the thoracic BMD is greater than that of lumber spine.[3,12] Therefore, we speculated that the ACR criteria may be not refer to thoracic BMD for osteoporosis/osteopenia diagnosis. Our results showed that the agreement of osteoporosis/osteopenia identification between BMD-T8-T10 and LBMD was moderate (kappa = 0.51),

which demonstrated that it is not a good choice to use raw thoracic BMD for osteopenia/osteoporosis diagnosis. Other methods should be considered.

The use of thoracic BMD for defining osteoporosis/osteopenia has not been well studied. Using the LBMD-based osteoporosis/osteopenia as a reference standard, we calculated the BMD-T8-T10 threshold for detecting osteopenia and osteoporosis. For osteopenia, the cutoff value was 138 mg/cm^3, and for osteoporosis, it was 97 mg/cm^3. When defining osteopenia or osteoporosis, the two cut-off points agreed well with those for LBMD (kappa = 0.74). Few studies have also shown the cut-off point of thoracic BMD for osteopenia or osteoporosis diagnosis. BMD thresholds at T8 (126.6 mg/cm^3 for osteopenia and 94.1 mg/cm^3 for osteoporosis), T9 (128.8 mg/cm^3 for osteopenia and 95.4 mg/cm^3 for osteoporosis) and T10 (131.0 mg/cm^3 for osteopenia and 95.0 mg/cm^3 for osteoporosis) were reported for defining osteoporosis/osteopenia.[8] The cut-off point for osteoporosis in our study was close to the published data. However, the performance of those cut-off points was not tested. Moreover, that study only showed cut-off point of a single vertebral body. To our knowledge, the thresholds of combined T8, T9 and T10 were not reported. Furthermore, a linear regression equation was used to obtain the cut-off point.[8] ROC curve, which is frequently used to determine the ideal cut-off point, was utilized to calculate the thresholds in our study. It is vital to verify the efficacy of this strategy.

Low-dose CT for lung cancer screening has gradually increased over the past decade. The age of lung cancer onset and the age of osteoporosis onset have overlap. The US guideline recommended that adults aged 50 to 80 years with high-risk should undergo annual screening for lung cancer.[13] China guideline also recommended that those subjects older than 50 years should undergo such screening.[14] Moreover, lung cancer screening is recommended for individuals with chronic obstructive pulmonary disease, which usually occurs in older person in China.[15] Every year, a large number of middle-aged and elderly people undergo lung CT cancer screening in China. Osteoporosis/osteopenia identification during CT scans did not increase radiation exposure or scanning time. Several studies have demonstrated that cardiac CT could be used for identifying individuals with low bone mass or with a high risk of fracture.[2,16] Our study calculated the threshold of BMD-T8-T10 for osteoporosis/osteopenia identification, which may be used to diagnose osteoporosis during CT lung scans and cardiac CT.

Our study also has several limitations. First, the sample size was relatively small. Our results might need to be validated in studies with large sample sizes. Second, we only calculated the cut-off point of BMD-T8-T10 because cardiac CT usually scans such sections and our results may be extended to those subjects who underwent cardiac CT because chronic coronary diseases are also highly prevalent in older adults. In addition, our results and those of a recent study both showed that the BMD of T8, T9 and T10 were relatively close.[17] Third, our study included only subjects older than 50 years because people of these ages are recommended to undergo CT lung cancer screening. Future research is needed to determine whether our findings can be applied to younger adults. Fourth, subjects who were taking drugs affecting bone metabolism and those who had a history of surgery, tumors, ankylosing spondylitis or chronic diseases affecting bone metabolism were excluded. However, we cannot exclude all pharmacological therapies and comorbidities that may affect bone. Finally, it has been shown that thoracic BMD is related to fracture risk.[18] However, we did not show the role of our methods in predicting fracture risk.

In conclusion, our research demonstrated that the ACR criteria for may not be appropriate for BMD-T8-T10 for identifying osteoporosis/osteopenia. In the present study, we obtained two cut-off point for osteoporosis/osteopenia diagnosis based on BMD-T8-T10: 97 mg/cm^3 for osteoporosis, 138 mg/cm^3 for osteopenia. In addition, translating BMD-T8-T10 to LBMD is also useful for identifying osteoporosis/osteopenia. Based on information on the translated LBMD and the BMD-T8-T10 cut-off point, the two methods demonstrated good diagnostic performance in detecting osteoporosis. To determine generalizable BMD-T8-T10 thresholds for osteoporosis, more research is needed.

Ethics Approval and Consent to Participate

This study conformed to the ethics principles set forth by the Declaration of Helsinki. This retrospective study was approved by the Institutional Ethics Review Board of the Affiliated Hospital of Nanjing University of Chinese Medicine. Informed consent was waived by Institutional Review Board of the Affiliated Hospital of Nanjing University of Chinese Medicine because of the retrospective design. All patient data were anonymized.

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Disclosure

The authors report no conflicts of interest in this work.

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