ORIGINAL RESEARCH

The Suitable Population for Opportunistic Low Bone Mineral Density Screening Using Computed Tomography

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Objective: To explore the suitable population of CT value for predicting low bone mineral density (low-BMD).

Methods: A total of 1268 patients who underwent chest CT examination and DXA within one-month period retrospectively analyzed. The CT attenuation values of trabecular bone were measured in mid-sagittal plane from thoracic vertebra 7 (T7). Receiver operating characteristic (ROC) curves were used to evaluate the ability to diagnose low-BMD.

Results: The AUC for diagnosing low BMD was larger in women than in men (0.894 vs 0.744, p < 0.05). The AUC increased gradually with the increase of age but decreased gradually with the increase in height and weight (p < 0.05). In females, when specificity was adjusted to approximately 90%, a threshold of 140.25 HU has a sensitivity of 69.3%, which is higher than the sensitivity of 36.5% in males for distinguishing low-BMD from normal. At the age of 70 or more, when specificity was adjusted to approximately 90%, a threshold of 126.31 HU has a sensitivity of 76.1%, which was higher than that of other age groups.

Conclusion: For patients who had completed chest CTs, the CT values were more effective in predicting low-BMD in female, elderly, lower height, and lower weight patients.

Keywords: bone mineral density, chest computed tomography, dual-energy X-ray absorptiometry, attenuation value

Introduction

It is projected that by 2050, the incidence of osteoporotic fractures in China will surpass a staggering 5.9 million cases, with medical expenditures soaring above the astounding sum of 20 billion dollars.[1,2] At present, lumbar and hip dual-energy X-ray absorptiometry (DXA) is the most commonly used reference standard for the diagnosis of osteoporosis.[3–5] However, over 80% of patients with osteoporotic fractures do not undergo bone mineral density (BMD) testing to reduce the risk.[6] Since DXA still has some limitations, fragility fractures also occur in patients with osteopenia defined by DXA.[6,7] Therefore, more sensitive measures are needed to identify people at low and high risk for osteoporotic fractures.[8]

It has been reported that the attenuation value of Hounsfield unit (HU) expression in trabecular (non-cortical) vertebrae scanned by computed tomography (CT) can correctly reflect BMD. The utility of vertebral CT attenuation value derived from CT is used to detect low bone mineral density (low-BMD), which has been confirmed.[9,10] Reduced CT attenuation value can be used as a basis for detecting decreased BMD. Furthermore, the advantage of CT attenuation value in assessing fracture risk, implant stability, and spinal fusion compared to DXA has been studied. Previous studies found that the CT attenuation value of 7th thoracic vertebra (T7) is highly correlated with osteoporosis.[11,12] Meanwhile, studies have found that T7-T8 thoracic vertebrae have a higher risk of fracture.[13] CT scans can identify vertebral compression fractures from reconstructed sagittal images, providing an opportunity for detection and proper management. Chest CT scan is widely used

in the screening of lung cancer and follow-up of pulmonary nodules, and its images carry valuable potential information about vertebral quality, especially sagittal images, which play an important role in the evaluation of vertebral morphology.[14–16] However, the optimal population of low bone mineral density predicted by CT has not been defined in the previous literature. This study fills this gap by classifying the basic clinical characteristics of different populations.

The aim of this study is to use the attenuation value of the T7 on CT images and to explore its value in screening various types of people with low-BMD.

Materials and Methods

Study Participants

In this study, a total of 1867 patients were involved who were hospitalized in the General Medical Department and the Orthopedics Department and underwent DXA and chest CT from November 2020 to August 2021. This study was approved by the local Ethics Committee (IRB No. KY2022024). All procedures for this retrospective study were in accordance with the 1964 Helsinki Declaration and its later amendments. Informed consent was not required for this type of study. Then, 1268 patients were enrolled according to the following exclusion criteria: 1. Patients affected by bone metastases (such as renal and hepatic chronic diseases), mixed metabolic bone diseases, or acute high-impact trauma; 2. Previous primary or metastatic tumors, or vertebral fractures; 3. Calcified disc herniation area and cortical bone area were excluded; 4. An interval of more than 1 month between chest CT and DXA was excluded; 5. The use of contrast media in chest CT examination and other factors that may affect the CT attenuation value (Figure 1).

Dual Energy X-Ray Absorptiometry

DXA (Hologic Discovery) examinations of the lumbar spine (L1-L4) and/or femoral neck were performed by using a standard technique. Each patient's BMD was categorized based on the World Health Organization T-score classifications. The WHO criteria define a T-score of −1.0 to −2.5 as osteopenia, a T-score ≤-2.5 as osteoporosis, and a T-score ≥−1.0 as normal BMD. In the present study, low-BMD was defined as a T-score < −1.0 in the lumbar spine and/or femoral neck.

Computed Tomography

CT examinations were performed by using a 64-slice spiral CT scanner (Philips Ingenuity, the Netherlands). Scanning parameters: tube voltage: 120 kV, tube current: 30 mAs, layer thickness: 1.0 mm. Patients underwent chest CT in the supine position. Breath was held after inhalation, and the scan range was from the thoracic inlet to the level of the
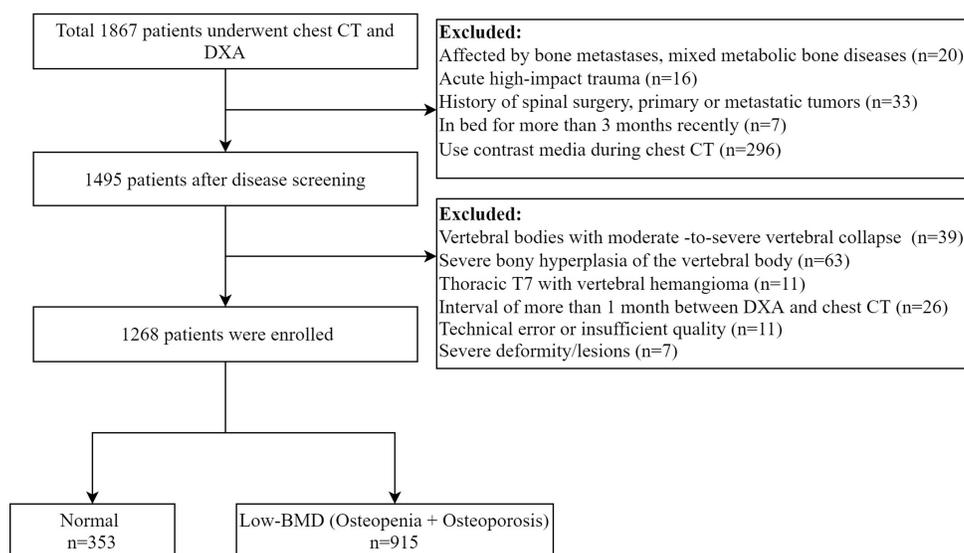

Figure 1 Flow diagram for screening patients.

costophrenic angle. In the Picture Archiving and Communication System (PACS), we locate T7 and look for the mid-sagittal plane. An oval area, excluding the cortical margin, was drawn on the mid-sagittal plane. While placing the region of interest (ROI), the posterior venous plexus area and vertebral shadow were avoided, and the average CT attenuation values of the ROI were measured (Figure 2). Manipulation was measured by two trained collectors who were unaware of the results.

Statistical Methods

All patients were divided into normal, low-BMD (osteopenia and osteoporosis) groups according to the T-score. Descriptive characteristics of the study population were tabulated as mean ± standard deviation or proportion. Chi-square test was used for differences of classification data. The scatter plot was drawn to calculate the regression coefficient R^2. Odds ratios were calculated with multivariate logistic regression. The area under curve (AUC), sensitivity, specificity, and Youden's index were calculated to screen for low-BMD. SPSS 22.0 (SPSS Inc., Chicago, IL, USA) and R (http://www.r-project.org) 4.2.1 software for Windows were used for statistical analysis. $P < 0.05$ was considered statistically significant.

Results

Clinical Baseline Characteristics

The study included 586 (46.2%) men and 682 (53.8%) women. The mean (±standard deviation) age for the entire sample was 59.02 (±11.65) years. A total of 915 patients (72.2%) had low-BMD. There were significant differences in sex, age, height, weight, T-score, and CT-T7 between normal and low-BMD groups ($p < 0.001$). Compared with the normal group, the proportion of women and elderly increased in the low-BMD group, while the proportion of high height and weight decreased. The CT-T7 was also decreased in the low-BMD group (Table 1).

In the scatter plots of different groups, we found that CT value and T-score had a better fit in female, advanced age, low height, and low weight. Scatter plots showed that the correlation coefficient R^2 between CT value and T-score was larger in women than in men (female: $R^2 = 0.510$; male: $R^2 = 0.319$ $p < 0.05$) (Figure 3). Meanwhile, we found that T-score was inversely proportional to age but positively proportional to high height and weight. The correlation coefficients R^2 between T-score and age, height, and weight were 0.114, 0.184, and 0.240 (Supplementary Figure 1).
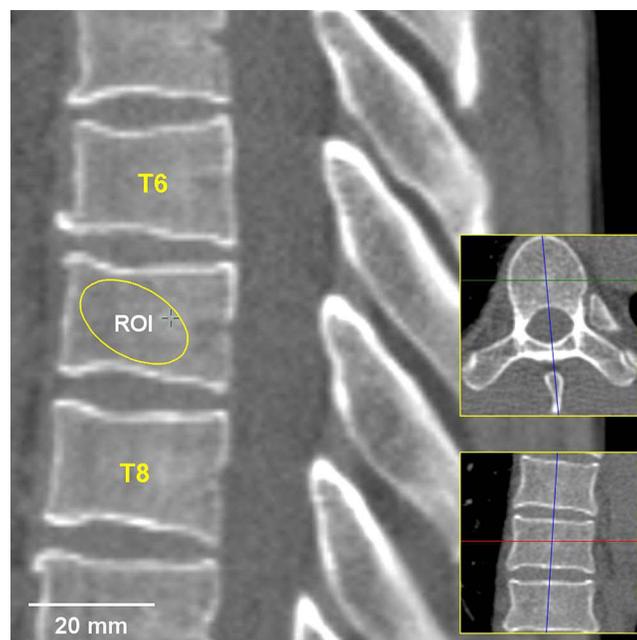

Figure 2 The 7th thoracic vertebra was located and the CT value of mid-sagittal plane was measured in the region of interest (ROI).

Table 1 Baseline Characteristics

Characteristics	Normal (n=353)	Low-BMD (n=915)	P
Sex, n (%)			< 0.001
Male	219 (62.0)	367 (40.1)	
Female	134 (38.0)	548 (58.9)	
Age, mean ± SD, years	57.16±11.85	62.88±11.02	< 0.001
Age, n (%)			< 0.001
<50	86 (24.4)	100 (10.9)	
50–59	116 (32.9)	247 (27.0)	
60–69	99 (28.0)	321 (35.1)	
≥70	52 (14.7)	247 (27.0)	
Height, mean ± SD, cm	166.62 ± 8.30	157.92 ± 8.62	< 0.001
Height, n (%)			< 0.001
≤150	18 (5.1)	173 (18.9)	
151–160	102 (28.9)	390 (42.6)	
161–170	151 (42.8)	276 (30.2)	
>170	82 (23.2)	76 (8.3)	
Weight, mean ± SD, kg	69.63 ± 12.00	60.13 ± 10.83	< 0.001
Weight, n (%)			< 0.001
≤50	11 (3.1)	183 (20.0)	
51–60	71 (20.1)	300 (32.8)	
61–70	113 (32.0)	292 (31.9)	
>70	158 (44.8)	140 (15.3)	
T-score, mean ± SD	−0.13±0.66	−2.42±0.93	< 0.001
CT-T7, mean ± SD, HU	196.18 ± 44.05	135.40 ± 44.11	< 0.001

Abbreviations: SD standard deviation; CT-T7, seventh thoracic CT; HU, Hounsfield unit; Low-BMD (osteopenia + osteoporosis).

Multivariate Logistic Regression Analysis

The low-BMD was regarded as the dependent variable, and univariate analysis of the factors for low-BMD was selected as independent variables (including sex, age, height, weight, CT-T7). It was found that female and advanced age were risk factors for low-BMD (female: OR = 1.420, 95% CI 0.953–2.117; age, ≥70 years: OR = 1.484, 95% CI 0.981–2.246), while high height, weight, and CT-T7 were protective factors for low-BMD (height, >160 cm: OR = 0.508, 95% CI 0.340–0.759; weight, >60 kg: OR = 0.403, 95% CI 0.290–0.561; CT-T7, >150 HU: OR = 0.089, 95% CI 0.059–0.133) (Table 2).

ROC Curves

CT-T7 (HU) was used as the test variable and low-BMD or not was used as the state variable to draw the ROC curve. Grouping by sex, age, height, and weight, it was found that the AUC of females was larger than that of males (0.894 vs 0.744, p < 0.05). The AUC increased gradually with the increase of age but decreased gradually with the increase in height and weight (p < 0.05).

In females, when specificity was adjusted to approximately 90%, a threshold of 140.25 HU has a sensitivity of 69.3%, which is higher than the sensitivity of 36.5% in males for distinguishing low-BMD from normal. At the age of 70 or more, when specificity was adjusted to approximately 90%, a threshold of 126.31 HU has a sensitivity of 76.1%, which was higher than that of other age groups. At the same time, it was found that the sensitivity and specificity gradually increased with age. Similar trends were found in subgroups of height and weight (Table 3) (Figure 4).

Discussion

Despite the WHO definition and therapeutic decision for osteoporosis still relying on the gold standard DXA results, the use of opportunistic CT as a screening tool identifying undiagnosed patients at high risk of fractures is without any doubt a tool that should be increasingly implemented in common practice, and may also replace the DXA in case the latter is
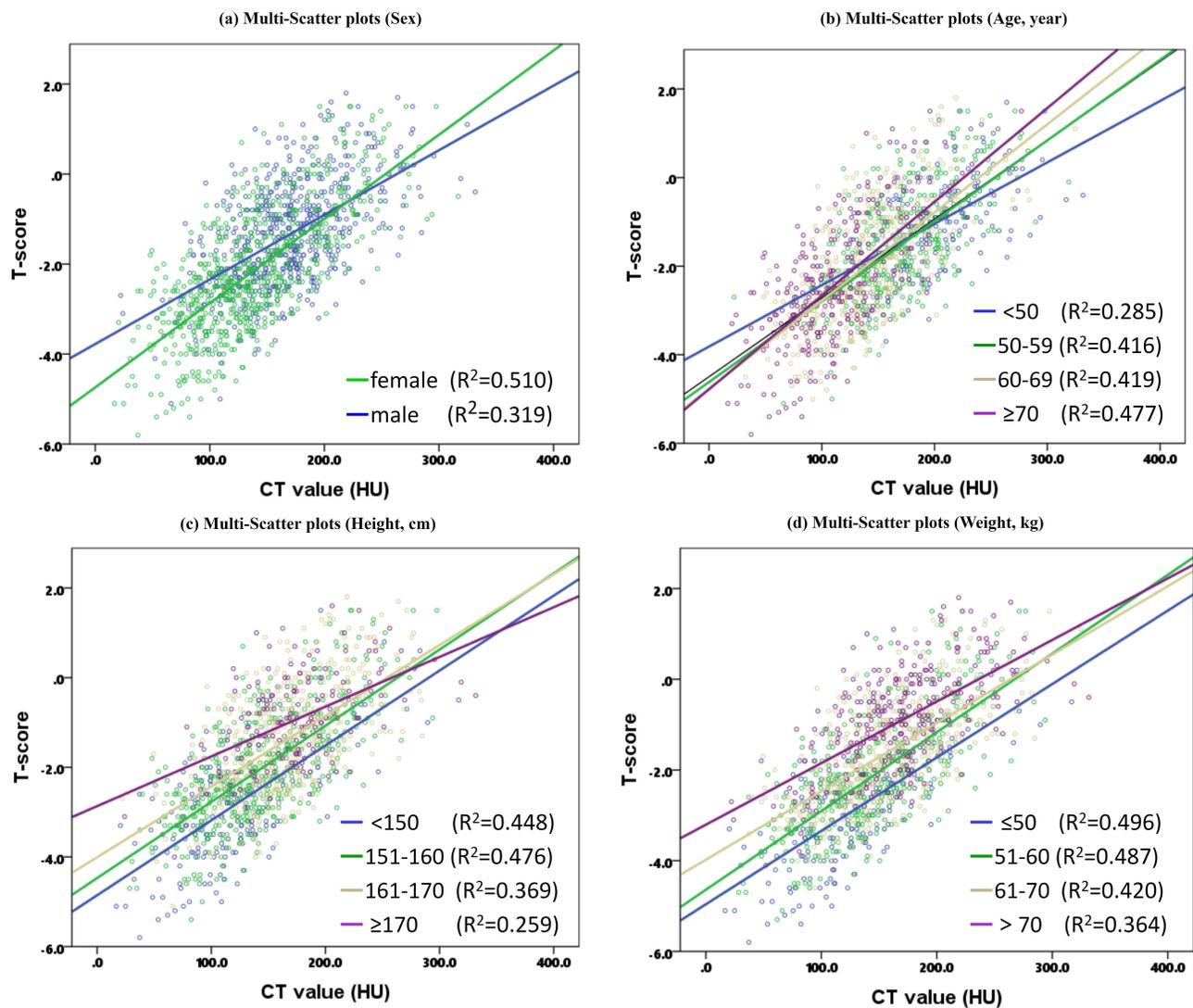
(a) Multi-Scatter plots (Sex)

(b) Multi-Scatter plots (Age, year)

(c) Multi-Scatter plots (Height, cm)

(d) Multi-Scatter plots (Weight, kg)

Figure 3 Scatter plot of the distribution of CT values and T-score. (**a**–**d**) show the different groups by sex, age height, and weight, respectively.

not feasible.[17–19] In this study, the average age of the patients was 59.02 years, and most of the patients used chest CT plain scans for COPD and lung cancer screening. Since the age of chest CT was close to the age of the high-risk patients of osteoporosis, and the parameters of chest CT were relatively fixed, the influence of voltage on attenuation value was avoided, making it likely to become the most economical and safe method for osteoporosis screening in the future.[20,21]

This study found a significant correlation between low-BMD from DXA and CT attenuation values of the thoracic spine from chest CT scans. Recently, the CT attenuation value of the thoracic vertebra in predicting osteoporosis has been

Table 2 Multivariate Logistic Regression Analysis

Variable	OR	95% CI	P value
Sex, female	1.420	0.953–2.117	0.085
Age, ≥ 70 years	1.484	0.981–2.246	0.062
Height, >160cm	0.508	0.340–0.759	0.001
Weight, >60 kg	0.403	0.290–0.561	<0.001
CT-T7, >150 HU	0.089	0.059–0.133	<0.001

Abbreviations: CT-T7, seventh thoracic CT; HU, Hounsfield unit; OR, odds ratio; CI, confidence intervals.

Table 3 The Performance of Predicting Low Bone Mineral Density Using Receiver Operating Characteristic (ROC) Curves Analysis

Variable	AUC (95% CI)	High Sensitivity (Approximately 90%)			High Specificity (Approximately 90%)			Youden's Index
		Threshold	SE (%)	SP (%)	Threshold	SE (%)	SP (%)	
Gender								
Male	0.744 (0.703–0.785)	202.82	90%	39.7%	141.95	36.5%	90%	0.355
Female	0.894 (0.866–0.921)	176.81	90%	67.9%	140.25	69.3%	90%	0.615
Age, years								
<50	0.747 (0.676–0.818)	233.68	90%	36.0%	167.66	29.0%	90%	0.433
50–59	0.809 (0.762–0.857)	201.61	90%	52.5%	150.71	44.8%	90%	0.479
60–69	0.822 (0.777–0.867)	172.55	90%	52.6%	130.76	50.6%	90%	0.486
≥70	0.914 (0.877–0.950)	145.69	90%	73.1%	126.31	76.1%	90%	0.691
Height, cm								
≤150	0.938 (0.899–0.977)	166.21	90%	77.8%	159.59	86.7%	90%	0.805
151–160	0.867 (0.830–0.904)	190.80	90%	61.8%	140.63	60.8%	90%	0.580
161–170	0.772 (0.725–0.818)	196.66	90%	47.7%	142.86	40.6%	90%	0.439
>170	0.722 (0.645–0.845)	196.65	90%	42.7%	140.36	36.8%	90%	0.345
Weight, kg								
≤50	0.943 (0.903–0.983)	179.32	90%	81.8%	172.61	87.4%	90%	0.825
51–60	0.900 (0.865–0.936)	189.97	90%	71.8%	149.64	67.7%	90%	0.652
61–70	0.791 (0.743–0.838)	194.64	90%	48.7%	139.68	48.3%	90%	0.431
>70	0.769 (0.716–0.821)	192.73	90%	44.3%	140.62	45.0%	90%	0.400

Abbreviations: AUC, area under the curve; CI, confidence intervals; SE, sensitivity; SP, specificity.

widely verified.[9,11,21,22] Romme et al[9] revealed a 147 HU threshold in predicting osteoporosis of average bone for these vertebrae (T4, T7, T10, L1). Meanwhile, Kim et al[8] reported that the threshold for men and women in predicting osteoporosis was 136.2 HU and 137.9 HU, respectively, from multilevel vertebrae (T4, T7, T10, L1). To explore the different cutoff points, by grouping the population, we found that different groups had different HU cutoff points. To distinguish between normal and low-BMD, we found that when the subject was younger than 50 years old and the threshold was 167.66 HU, the sensitivity was 29.0% and the specificity was 90%. However, when the subject was 70 years old or older and the threshold was 126.31 HU, the sensitivity was 76.1% and the specificity was 90%. At the same specificity in the two different age groups, we found not only a large difference in sensitivity (29.0% vs 76.1%) but also a difference of about 40 HU in the cutoff value between the two groups (167.66 HU vs 126.31 HU). When specificity was adjusted to approximately 90%, the patient's height ≤150 cm or weight ≤50 kg had higher sensitivity (86.7% and 87.4%). Therefore, we believed that vertebral CT attenuation value had higher diagnostic efficacy in predicting low-BMD in women, of advanced age, low height, and low weight.

In this study, we divided the patients into normal and low-BMD groups according to whether they had low-BMD or not. We constructed ROC curves to analyze the relationship between CT attenuation values and the diagnosis of low-BMD by grouping the population by gender, age, height, and weight. We were surprised to find that the diagnostic efficacy of CT attenuation values in females was higher than that in males (female: AUC = 0.894, 95% CI 0.866–0.921 vs male: AUC = 0.744, 95% CI 0.703–0.785). In the age group, the AUC area increased with age, and the sensitivity and specificity of predicting low-BMD also increased with age. Compared with younger patients, the CT cutoff points of older patients showed a gradually decreasing trend. However, this trend is quite the opposite in height and weight groups (Table 3). In conclusion, CT attenuation value has higher diagnostic efficacy in predicting low-BMD in women, older, and people with low height and weight. This also explains the reason why the same studies mentioned above produce different CT attenuation value cutoff points.

We found that the diagnostic efficacy of CT attenuation value in screening for low-BMD was improved in subjects with a low height or a low weight. Therefore, we cannot use BMI values alone to analyze the population. As we all know,
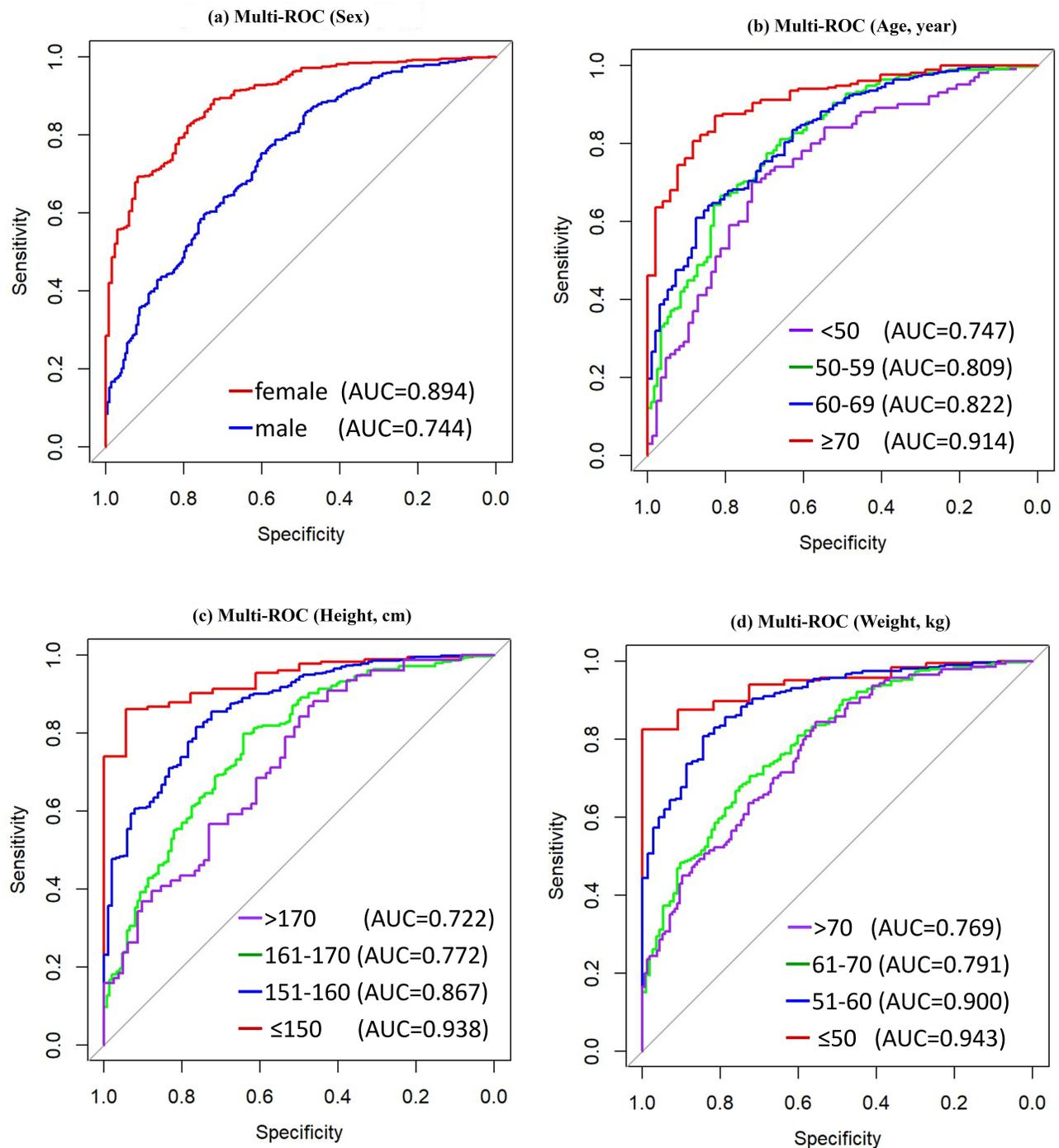
Figure 4 The receiver operating curve (ROC) curves of CT values in the diagnostic efficacy of low-BMD. (**a–d**) show the different groups by sex, age height, and weight, respectively.

BMI values can be obtained based on height and weight. It was calculated by the formula: BMI = weight (kg)/height (m)². In this study, the CT attenuation value is more suitable for predicting low-BMD in people with low height and weight, and the numerator and denominator values are smaller according to the BMI formula, so BMI performance does not apply to this study.

This study is the first to analyze CT attenuation value in predicting low-BMD population, and the results show that CT attenuation value is more suitable for women, of advanced age, low height, and weight patients to predict low-BMD. This method is not only more in line with individual characteristics but also can greatly improve the diagnostic efficiency

of low-BMD. The CT attenuation value of each region or different population needs to be adjusted according to different situations. It is worth noting that we grouped according to different populations and finally found the best population for chest CT opportunistic screening for low-BMD. This is the rule, and it applies to most regions.

Confirmation of low-BMD findings with DXA and estimation of fracture risk with BMD plus clinical fracture risk factor assessment is the current standard of care. A recent position statement of the National Bone Health Alliance recommends that osteoporosis be diagnosed not only by low-BMD T-score but also by elevated fracture risk.[23] Fracture risk assessment has recently been increasingly recommended.[24] Therefore, regardless of the definition of CT attenuation value, we should perform opportunistic screening for individuals with a potentially increased risk of fracture. In this study, the sagittal plane can effectively screen out the presence of vertebral compression fracture, and it also greatly saves the reading time of radiologists compared with the axial plane CT attenuation value measurement. Compared with previous studies on the CT attenuation value of the vertebral body for predicting osteoporosis, our opportunistic screening method can greatly improve the diagnostic performance, and its benefit potential is great.[25]

Sagittal CT measurements of the thoracic spine not only require no additional equipment but also require no additional cost and time for the patient.[26,27] By combining attenuation measurement and vertebral fracture assessment into the sagittal view, a doctor can potentially identify patients who may be at high risk for developing fragility fractures.[25,28,29] In addition, both the data collectors and data analysts in this study were unaware of the grouping of participants, which could effectively avoid artificial subjective errors.

This study has several limitations. First, the CT attenuation value of T7 was obtained by opportunistic screening chest CT scan. Compared with quantitative computed tomography, CT attenuation values may be affected by the surrounding soft tissue. Second, among a lot of patients with osteopenia and osteoporosis, the patients who used chest CT plain scans are limited.

In conclusion, this study found that the sagittal CT attenuation of the thoracic vertebral body has high diagnostic efficacy in predicting low-BMD. Furthermore, by grouping, we found that vertebral CT attenuation value was more effective in predicting low-BMD in female, elderly, lower height, and lower weight patients. For patients who had completed chest CT, doctors can potentially identify patient who may be at high risk for developing fragility fractures by using sagittal reconstruction of chest CT. It can achieve early screening and early diagnosis.

Ethical Approval

This study was approved by the institutional review board of the First Hospital of Nanchang in compliance with the Helsinki and an exemption from the informed consent was obtained (IRB No. KY2022024). All data were anonymized before the analysis to safeguard patient privacy.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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