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Letters to the Editor

Bone mineral density at the ankle measured with quantitative CT (QCT)

Osteoporosis is an important public health problem globally *(1)*, especially in elderly individuals and postmenopausal women. Osteoporotic fractures result in poor quality of life, significant mortality, and a heavy economic burden *(1-4)*. Bone mineral density (BMD) is an intrinsic property of bone that reflects bone health and is important in the diagnosis of osteoporosis and the prevention of osteoporotic fractures *(5,6)*. Although ankle fractures are reported to be one of the most common types of osteoporotic fractures in individuals aged > 50 years *(7-11)*. few studies have used quantitative computed tomography (QCT) to measure trabecular bone in the ankle joint *(12)*. We report a pilot study to investigate the feasibility and repeatability of QCT measurements of volumetric bone mineral density (vBMD) in the distal tibia, talus, and calcaneus.

The Ethics Committee of the Hospital approved the protocol, and all patients gave written informed consent for their data to be used for research purposes. The participants were all the ankle injury patients admitted to the trauma centre of the Hospital between June 15 and July 15, 2021, and prescribed an ankle CT examination. Exclusion criteria were renal dysfunction, diabetes mellitus, hyperparathyroidism, or a drug history that impacted bone metabolism. Patients with fractures in both ankle joints were excluded. In total, 311 patients (189 men and 122 women) were enrolled in the study. Baseline demographic characteristics (age, height, and weight) were evaluated by questionnaire.

All participants underwent a routine CT scan of both ankles from 10 cm above the styloid process of the fibula to the bottom of the calcaneus (uCT40, United Imaging, China). The scan parameters were 120 kV, 100 mAs, 1 mm thickness, and a 30 cm field of view. A QCT calibration phantom (Mindways Software Inc., Austin, TX) was placed beneath the ankles and scanned simultaneously. The spine module of the QCT software was used to measure vBMD in the ankle. If both ankle joints were normal, the right ankle was measured, and if only one was broken, the healthy ankle was measured. Three regions of interest (ROI) were drawn in each ankle (Fig. 1). The measurements were made by two radiologists with 5 and 8 years of experience, respectively.

Data was analyzed using SPSS v25.0 (IBM, Inc., Armonk, New York). Two-sample t-tests and Wilcoxon rank-sum tests were used to compare demographic characteristics and vBMD measurements between men and women for Gaussian and non-Gaussian variables, respectively. Participants were divided into four age groups (≤20; 21-40; 41-60 and >60 years) and vBMD was compared between men and women. Pearson correlation coefficients between vBMD, age, and BMI were

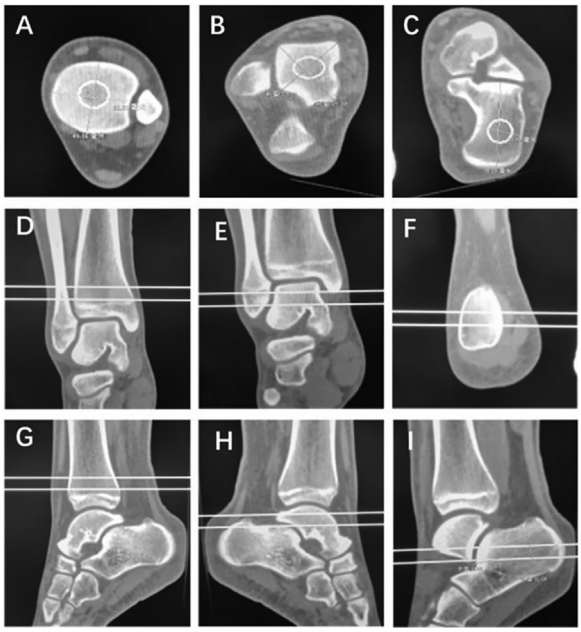

Fig. 1. A, D, and G show the placement of the ROI in the distal tibia; B, E and H show the placement in the talus; C, F, I show the placement in the calcaneus. The distal tibia ROI was placed at the geometric center of the bone in the transverse plane, 5 mm above the epiphyseal plate. The talus ROI was set at the intersection of two diagonals in the transverse plane and beneath the articular surface. The calcaneus ROI was selected at the slice above the calcaneal tubercle, and the intersection of the long axis and short axis was chosen as the center of the ROI in the transverse plane, and the mid plane of the calcaneus was selected in the coronal and sagittal projections. The cross-sectional area of each ROI was 220±10 mm^2 and the depth 9 mm in every participant, and cortical bone and any abnormalities were excluded.

Table 1
Demographic characteristics and vBMD in participants.

Parameter	Men (N=189)	Women ($N = 122$)	[a]p Value
Age (years)	38.0±16.0	43.7±18.9	0.006
Height (m)	1.75 (0.08)	1.63 (0.09)	<0.001
Weight (kg)	75.0 (12.5)	62.0 (10.0)	<0.001
BMI (kg/m^2)	24.2 (3.8)	23.9 (4.3)	0.162
Tib vBMD (mg/cm^3)	168.1±56.7	159.3±47.3	0.157
Tal vBMD (mg/cm^3)	270.1±56.1	257.5±51.2	0.047
Cal vBMD (mg/cm^3)	122.8±42.2	118.5±40.4	0.371

Values are unadjusted mean ± SD or median with interquartile, unless indicated otherwise;
[a]*P*-values are for comparison of characteristics between male and female participants;BMD: bone mineral density; BMI: body mass index; Tib: tibia; Tal: talus; Cal: calcaneus.

evaluated, along with the correlations between the vBMD measurements. Statistical significance was set at a two-sided P-value of <0.05. Sixty-nine randomly selected participants were measured by both radiologists, and the inter-observer reproducibility of the vBMD measurements was assessed by the root mean square standard deviation (RMS SD) *(13)*.

The demographic characteristics of the 189 male and 122 female participants are listed in Table 1. The men were significantly younger, taller, and heavier than the women. Mean vBMD was similar in men and women in the distal tibia (p=0.157) and calcaneus (p=0.371), although men had a higher mean vBMD in the talus than women (p=0.047). In most age groups, the mean vBMD of the distal tibia, talus, and calcaneus was similar between men and women (Table 2). However, in the youngest group (≤20 years old), men had higher vBMD of the talus than women (p=0.046), and in the oldest group (age >60 years), vBMD of the calcaneus in men was also higher than in women (p=0.029). vBMD of the distal tibia decreased significantly with age in both men (r = -0.353, $p < 0.001$) and women (r = -0.414, $p < 0.001$) (Table 2). vBMD of the calcaneus was also correlated with age in both sexes (r = -0.422, $p < 0.001$ and r = -0.546, $p < 0.001$, respectively). In both sexes, there was only a weak correlation between age and talus vBMD (r = -0.033, $p = 0.649$ and r = -0.134, $p = 0.142$, respectively). In men, talus vBMD remained high in all age groups, while in women, the peak value was at age 41-60 years, followed by a decline. In comparison, the vBMD of the distal tibia and calcaneus decreased progressively with age. There was no significant correlation between vBMD and BMI at any of the three measurement sites in either sex.

In men, vBMD of the talus correlated best with the calcaneus ($r = 0.503$, $p < 0.001$), followed by the correlation between the distal tibia and the calcaneus ($r = 0.495$, $p < 0.001$), and then the correlation between the distal tibia and talus vBMD ($r = 0.422$, $p < 0.001$). In women, the correlations were similar (talus vs. calcaneus: $r = 0.499$, $p < 0.001$; distal tibia vs. calcaneus: $r = 0.417$, $p < 0.001$; distal tibia vs. talus: $r = 0.308$, $p = 0.001$).

In the reproducibility study, Bland-Altman analysis revealed no inter-observer bias for either the distal tibia, talus, or calcaneus vBMD (p=0.946, 0.133, and 0.752, respectively). The RMS SD was 14.6, 21.8, and 15.6 mg/cm^3, respectively.

This pilot study produced several useful findings. First, trabecular vBMD measured by QCT at sites in the ankle

Table 2
vBMD in Male and female participants in different age groups.

vBMD site	Age (years)	Men		Women		[a]p Value
		N	vBMD (mg/cm^3)	N	vBMD (mg/cm^3)	
Tibia	≤20	29	192.9±26.9	17	186.7±25.0	0.442
	21-40	82	182.1±61.4	38	180.4±40.4	0.876
	41-60	59	145.3±52.8	42	146.7±39.7	0.886
	>60	19	140.4±46.2	25	130.0±57.2	0.521
Talus	≤20	29	268.7±51.2	17	238.1±44.1	0.046
	21-40	82	272.3±45.4	38	273.4±40.3	0.894
	41-60	59	273.0±65.0	42	276.4±40.3	0.751
	>60	19	253.4±74.6	25	214.8±58.8	0.062
Calcaneus	≤20	29	158.3±44.3	17	153.9±32.1	0.727
	21-40	82	126.7±35.5	38	129.7±36.5	0.671
	41-60	59	105.6±41.2	42	117.3±25.4	0.082
	>60	19	105.1±31.7	25	79.3±41.3	0.029

Values are unadjusted mean ± SD.
[a]*P*-values are for comparison of vBMD between male and female participants.N: number of participants; vBMD: volumetric bone mineral density.

showed good reproducibility, confirming that QCT is a suitable tool for measurements in the ankle. Second, in both sexes, vBMD of the distal tibia and calcaneus correlated negatively with age. Third, in both sexes, vBMD measurements at the distal tibia, talus, and calcaneus correlated moderately with each other. These findings have improved our understanding of QCT vBMD measurements in the ankle. Our study also had several limitations. To reduce radiation exposure, we did not perform QCT scans of the lumbar spine and proximal femur. Therefore, we were unable to evaluate the relationship between vBMD measurements at the ankle and the central skeleton. Additionally, there was no long-term follow-up, and thus the value of ankle vBMD measurements for predicting future fractures could not be evaluated. In conclusion, QCT shows good reproducibility for measuring vBMD in the ankle. Its low radiation dose and good precision may make it a suitable tool for quantifying BMD at peripheral sites. Future studies should focus on its potential role in osteoporosis diagnosis.

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Declaration of Competing Interest

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[#]Compliance with ethical standards; Ethical approval for this study was obtained by the Research Ethics Committee of the Jishuitan Hospital