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NORMATIVE DATA FOR PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (pQCT) BONE PARAMETERS IN VIETNAMESE MEN AND WOMEN

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Background: *Peripheral quantitative computed tomography (pQCT) differentiates between cortical and trabecular bone mineral density (BMD), is better at fracture prediction than areal BMD.* ***Objectives:*** *To develop sex- and age specific- normative reference data for pQCT derived bone parameters for Vietnamese men and women.* ***Materials and methods:*** *The reference range was constructed with 2152 healthy individuals (1319 women and 833 men) from the Vietnam Osteoporosis Study aged 18 years and older. Bone parameters at 4% and 66% positison of the radius and tibia was measured by pQCT (XCT 2000, Stratec Medizintechnik, Pforzheim, Germany). The reference curves for each parameter were constructed using the Generalized Additive Model for Location Scale and Shape modeling technique. The peak ages for these parameters were determined from change point analysis based on change of mean.* ***Results:*** *Women had a slightly higher mean age compared to men (46 vs. 43 years). As expected, men demonstrated a greater BMI than that of women (23.2 vs. 22.5 kg/m²). About 7.0% of women and 9.4% of men were categorized as obese. Overall, pQCT bone parameters were higher in men than in women. The timing of peak bone parameters varied by skeletal sites: at the radius 4% position, peak vBMD occurred earlier for women than for men (24 vs. 30 years old), whereas at the tibia 4% position, both women and men achieved peak value at an earlier age (before 18 vs. 26 years old).* ***Conclusion:*** *This study provides gender- and age-specific normative reference data for pQCT bone variables in the Vietnamese population, serving as a valuable resource for interpretation, benefiting not only physicians but also the public.*

Keywords: *Peripheral quantitative computed tomography (pQCT), bone mineral density (BMD), normative reference data, Vietnamese population, gender differences, age-related changes.*

I. BACKGROUND

Osteoporosis is recognized as one of the major public health problems which has been affecting more than 200 million people globally. It is a skeletal disorder characterized by low bone mass, deterioration of bone tissue, and disruption of bone microarchitecture, which leads to compromised bone strength and elevates the risk of fragility fractures. The Dual Energy X-ray Absorptiometry (DXA) scans are used to measure areal bone mineral density (aBMD) to classify osteoporosis. However, half of fractured individuals arise from those who do not meet the aBMD criteria for osteoporosis. This is because diabetes, chronic kidney disease, and hyperparathyroidism, under medication treatment, tend to affect the skeletal micro-architecture, which DXA cannot capture [1]. Technologies have been developed to assess bone quality, and peripheral quantitative computed tomography (pQCT) is one of them. The pQCT can measure volumetric bone mineral density (vBMD) at the radius and tibia and separates bone parameters into trabecular and cortical bone compartments. Unlike aBMD, vBMD accounts for bone thickness and orientation. It is known that vBMD is associated with prior fractures at both the radius and tibia [2]. Furthermore, vBMD was superior to aBMD in identifying vertebral fracture [3]. Most studies assessing pQCT parameters have focused on older adults, with limited reference data across the lifespan. Reference ranges of bone parameters have been constructed but no studies have explored sex- and age-related differences in pQCT parameters, particularly in Asians [4]. This study aimed to develop sex- and age-specific normative reference data for pQCT-derived bone parameters for Vietnamese men and women. This serves as a valuable resource for interpretation, benefiting not only physicians but also the public.

II. MATERIALS AND METHODS

2.1. Materials

This research is a part of the Vietnam Osteoporosis Study (VOS), in which protocol and procedures have been described elsewhere [5]. The research and ethics committee of People's Hospital 115 approved the study's protocol (no. 297/BV-NCKH, 6th August 2015), adhering to the ethical principles of the Declaration of Helsinki. All participants provided written informed consent. Participants were recruited randomly via a random computer-based selection and recruitment from universities.

2.2. Methods

Data collection for this study involved a structured questionnaire and electronic equipment. Trained interviewers assisted participants in filling out the questionnaire, which gathered information on demographics, lifestyle, nutrition, and medical history. Height and weight were measured using an electronic portable, wall-mounted stadiometer (Seca Model 769; Seca Corp, CA, USA) without shoes, accessories, hats, or heavy clothing. BMI was calculated as the weight in kilograms divided by the square of the height in meters (kg/m^2). Cortical and trabecular vBMD measurements were performed at 4% and 66% of the non-dominant tibial length using pQCT (XCT 2000, Stratec Medizintechnik, Pforzheim, Germany). We focused on distal trabecular density (mg/cm3), proximal cortical density (mg/cm^3), cortical thickness (mm) and polar stress and strain index (mm^3).

Separate sample size calculations were performed for each of the gender. No previous studies have published data on normative reference ranges for pQCT for both genders. Calculations were based on previous studies providing mean (μ) and standard deviation (σ) for each gender. Specifically, we extracted the statistics for total bone density of the distal radius in Japanese women [6] (μ = 405, σ = 62) and total area of the distal radius in Australian men [7] (μ = 1329, σ = 154) to estimate the required sample sizes. The calculation for women and men were performed using the formula to estimate population mean, $n = \left(\frac{z_{\alpha/2}\sigma}{E}\right)^2$, where $z_{\alpha/2}$is the critical value from the standard normal distribution for a desired 95% confidence level (hence $z_{\alpha/2} = 1.96$). The margin of error, E, representing the maximum allowable difference, was set at $0.01 \times \mu$. Based on these calculations, we estimated that at least 890 healthy women and 516 healthy men are needed for this study. A total of 4157 participants were enrolled, with 3355 undergoing pQCT scans for both the radius and tibia. Of these, 2152 individuals (1319 women and 833 men) with no specific diseases were considered for analysis.

Sex- and age-specific references were created using the General Additive Model for Location Scale and Shape (GAMLSS). All statistical analyses were conducted using the R statistical environment. The estimation of model parameters was performed using the "gamlss" package. In an exploratory analysis, we observed the relationships between pQCT parameters and age, stratified by sex. We analyze the change points of pQCT parameters using the "segmented" package.

III. RESULTS

3.1. Participants characteristic

Table 1. Baseline characteristic for 1319 women and 833 men

Parameter	All (n = 2152)	Women (n = 1319)	Men (n = 833)	p-value
Age (years)	44.7 ± 14.8	45.8 ± 14.6	43.1 ± 15.0	<0.001
Age group, n (%)				0.001
18-29	462 (21.5%)	251 (19.0%)	211 (25.3%)	
30-39	321 (14.9%)	178 (13.5%)	143 (17.2%)	
40-49	457 (21.2%)	298 (22.6%)	159 (19.1%)	
50-59	571 (26.5%)	364 (27.6%)	207 (24.8%)	
60-69	259 (12.0%)	171 (13.0%)	88 (10.6%)	
70+	82 (3.8%)	57 (4.4%)	25 (3.0%)	
Weight (kg)	56.6 ± 9.1	53.0 ± 7.6	62.4 ± 8.4	<0.001
Height (cm)	158.2 ± 7.8	153.9 ± 5.4	165.0 ± 5.8	<0.001
BMI (kg/m^2)	22.8 ± 3.2	22.5 ± 3.2	23.2 ± 3.1	<0.001
Obese, n (%)	170 (7.9%)	92 (7.0%)	78 (9.4%)	0.001

Values are mean ± standard deviation or number and percentage. p-values were derived from unpaired t-test (for continuous variables) or chi-squared test (for categorical variables).

Detailed participant characteristics are provided in Table 1. On average, women were older than men (46 vs 43 years). As expected, men weighted more and taller than women, with a BMI approximately 0.7 kg/m² higher (23.2 vs. 22.5 kg/m²; $p < 0.001$). About 7.0% (n = 92) of women and 9.4% (n = 78) of men were categorized as obese.

3.2. Trabecular density, mg/cm3

Table 2. pQCT parameters for 1319 women and 833 men

	Parameter	All (n = 2152)	Women (n = 1319)	Men (n = 833)	p-value
Radius 4%	Total density (mg/cm^3)	342.2 ± 68.5	322.9 ± 66.9	372.8 ± 59.4	<0.001
	Trabecular density (mg/cm^3)	172.6 ± 48.3	153.5 ± 42.0	203.9 ± 40.9	<0.001
Radius 66%	Total density (mg/cm^3)	710.2 ± 110.2	703.2 ± 119.0	721.2 ± 93.8	<0.001
	Cortical density (mg/cm^3)	1119.6 ± 53.2	1117.7 ± 58.0	1122.5 ± 44.8	0.034
	Cortical thickness (mm)	2.0 ± 0.4	1.8 ± 0.4	2.2 ± 0.4	<0.001
	Polar stress-strain index (mm^3)	228.1 ± 73.1	190.4 ± 48.2	290.7 ± 63.8	<0.001

	Parameter	All (n = 2152)	Women (n = 1319)	Men (n = 833)	p-value
Tibia 4%	Total density (mg/cm^3)	286.4 ± 47.7	275.8 ± 46.0	303.5 ± 45.5	<0.001
	Trabecular density (mg/cm^3)	207.2 ± 39.3	197.8 ± 36.5	222.5 ± 38.8	<0.001
Tibia 66%	Total density (mg/cm^3)	638.6 ± 81.1	636.7 ± 85.0	641.7 ± 74.4	0.156
	Cortical density (mg/cm^3)	1144.0 ± 36.6	1145.0 ± 41.1	1142.4 ± 28.3	0.096
	Cortical thickness (mm)	3.5 ± 0.6	3.4 ± 0.5	3.8 ± 0.6	<0.001
	Polar stress-strain index (mm^3)	1901.1 ± 493.2	1624.4 ± 303.8	2348.0 ± 404.6	<0.001

Values are mean ± standard deviation or number and percentage. p-values were derived from unpaired t-test.

Table 2 shows that men had higher trabecular density compared to women. The average difference between women and men was larger at the radius (154 vs. 204 mg/cm^3; $p < 0.001$) than at the tibia (198 vs. 223 mg/cm^3; $p < 0.001$). At the radius, women attained peak density before 18 years old and there is a reduction of 0.7 mg/cm^3 per year until age 48 (Figure 1a). There was an accelerated reduction period from 48 to 53, with a decrease of about 5.6 mg/cm^3 per year. For men, density gradually increased by 0.9 mg/cm^3 per year, reaching peak around 34 years old, then reduced by 4.1 mg/cm^3 per year until age 47 (Figure 1b). A similar trend was observed for women at the tibia, with peak density achieved before age 18 (Figure 3a). For men, peak density was also achieved before 18 years old, followed by a gradual decline of 0.7 mg/cm^3 per year, which accelerated from age 34 to age 42 at a rate of 5.7 mg/cm^3 per year (Figure 3b).

3.3. Cortical density, mg/cm3

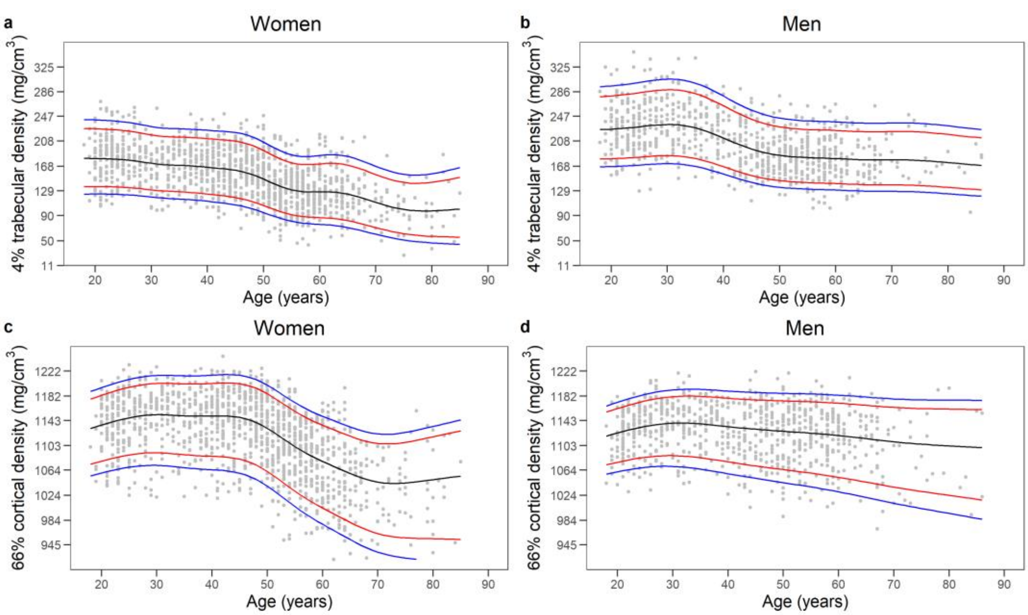

Figure 1. Age-related change of radial bone parameters for women (left) and men(right): a-b) Trabecular density at 4% position; c-d) 66% cortical density. The black line represents the median; the coloured lines represent 5, 10, 90, 95% percentiles for each age.

Men had slightly higher cortical density than women at the radius (1123 vs. 1118 mg/cm³; p = 0.034) but slightly lower at the tibia (1142 vs. 1145 mg/cm³; p = 0.096), both peaked around age 30. Women's radius cortical density stayed stable until age 46, then dropped by 5.3 mg/cm³ per year until stabilizing at age 68 (Figure 1c). In men, the decline was gradual after age 26 (Figure 1d). At the tibia, women's cortical density peaked around age 27 and stable to age 46, then rapidly decreased by about 5.9 mg/cm³ per year until age 58, after which the reduction decelerated to 2.0 mg/cm³ per year (Figure 3c). In men, tibial density gradually increased until age 35 at a rate of 1.0 mg/cm³ per year (Figure 3d). After that, the reduction in density was subtle at a rate of 0.5 mg/cm³ per year.

3.4. Cortical thickness, mm

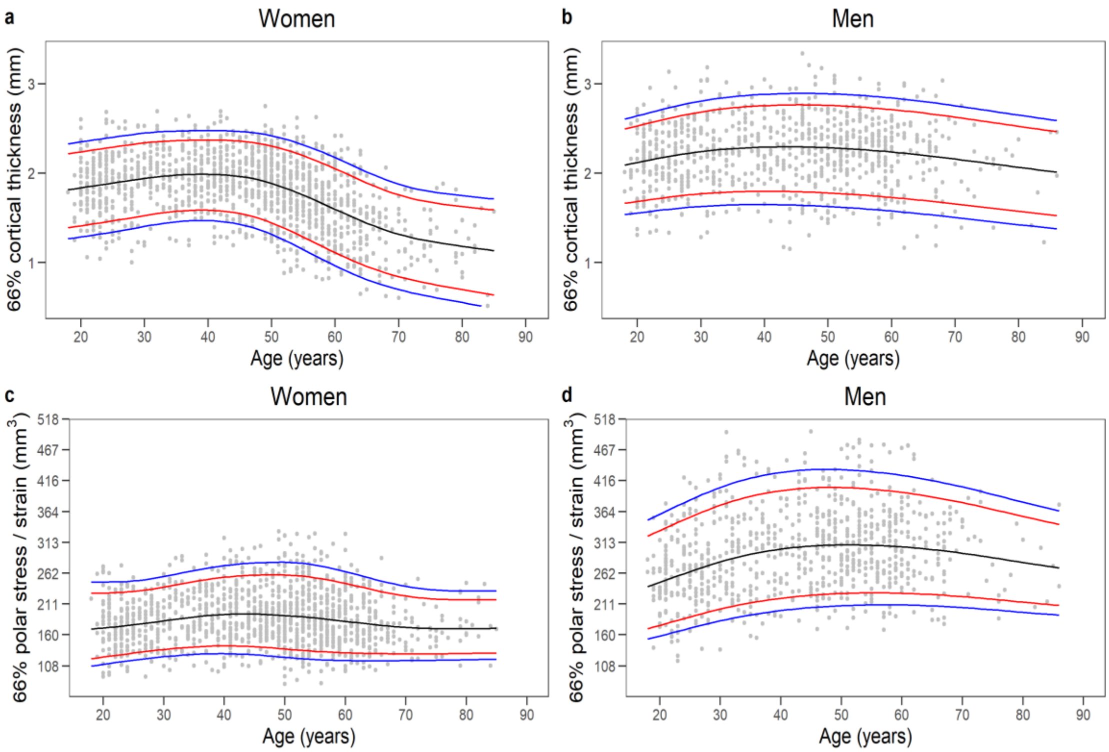

Figure 2. Age-related change of radial bone parameters for women (left) and men(right): a-b) 66% cortical thickness; c-d) 66% polar stress-strain index. The black line represents the median; the coloured lines represent 5, 10, 90, 95% percentiles for each age.

Overall, men had greater cortical thickness than women. The average difference was 0.4 mm: 1.8 mm in women versus 2.3 mm in men for the radius (p < 0.001), and 3.4 mm in women versus 3.8 mm in men for the tibia (p < 0.001). In women, the cortical thickness of the radius gradually increases at a rate of 0.01 mm, peaked at 47 years old, then a rapid reduction of 0.03 per year until 68 years old and stabilized (Figure 2a). However, at the tibia, after reaching the peak earlier at 36 years old at a rate of 0.01 mm per year, the cortical density rapidly reduced by 0.02 to 55 years old and further accelerated to a loss rate of 0.04 (Figure 3e). In men, for both radius and tibia, the degree of change was more subtle than in women. At the radius, men peak at 37 years old with a gain of 0.01 per year, then decrease by 0.004 per year (Figure 2b). At the tibia, the peak was attained earlier at 35 years old at a rate of 0.01, then a loss at the rate of 0.04 to 42 years old stabilized (Figure 3f).

3.5. Polar stress strain index, mm^3

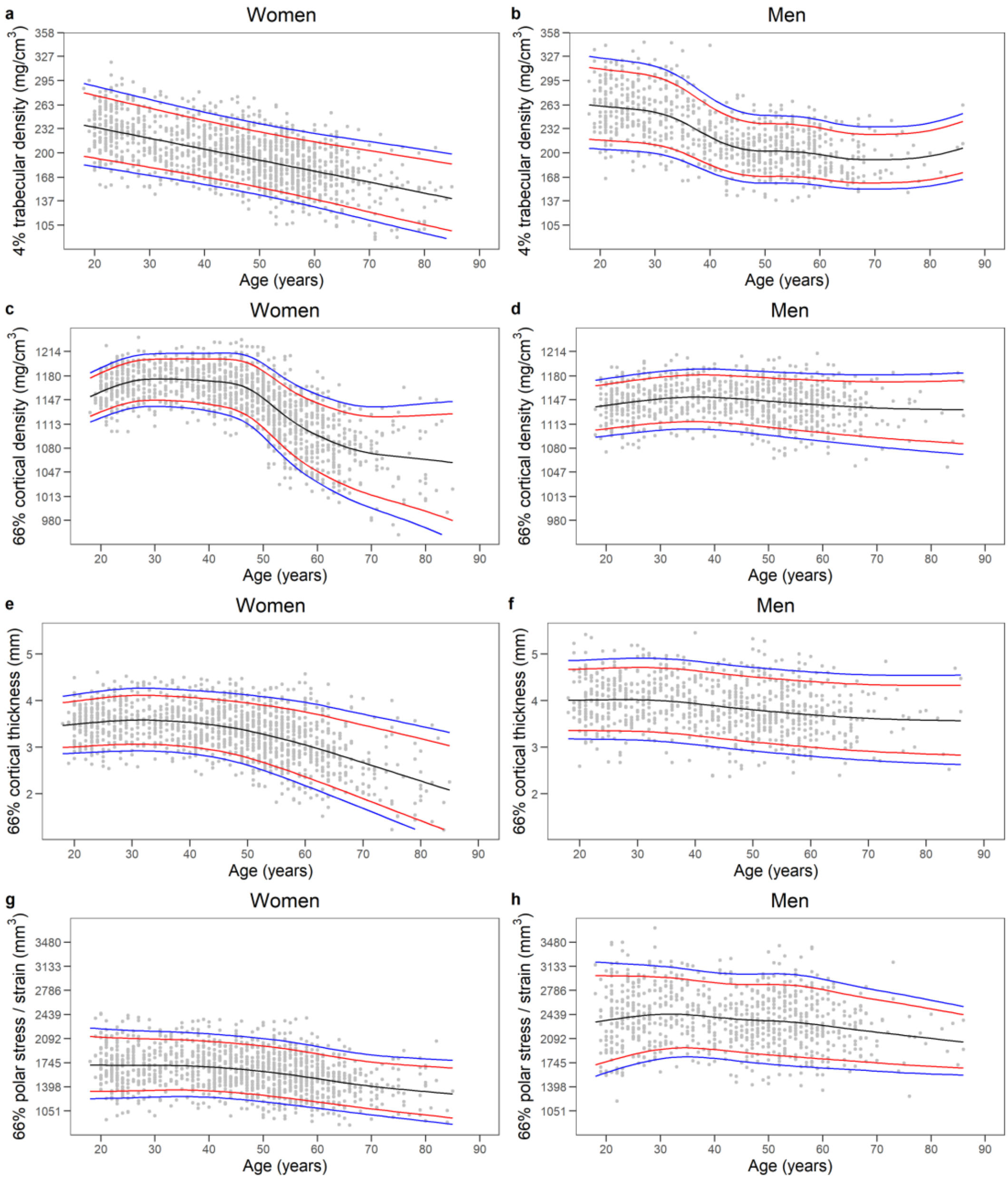

Figure 3. Age-related change of tibial bone parameters for women (left) and men(right): a-b) Trabecular density at 4% position; c-d) 66% cortical density; e-f) 66% cortical thickness; g-h) 66% polar stress-strain index. The black line represents the median; the coloured lines represent 5, 10, 90, 95% percentiles for each age.

Men had higher the polar stress-strain index than women at both radius (291 vs. 190; $p < 0.001$) and tibia (2348 vs. 1624; $p < 0.001$). In women, the radius index peaks at 42 years old, then reduces by a rate of 1.0 per year until stabilizing at 68 years old (Figure 2c). At the tibia, the peak occurred at 18 years old and stabilized until 35, then declined at 9.6 per year until 68, slowing to 7.3 per year after (Figure 3g). In men, the trend was different between radius and tibia. At the radius, the index increased gradually at a rate of 4.9 until it peaked at 31 years old, then decelerated at a rate of 0.5 until 62 years old and then reduced at a rate of 2.1 (Figure 2d). At the tibia, the index follows a bimodal trend where it first gained with a rate of 15.4 until 34 years old, then reduced at a rate of 22.7 until 47 and stabilized until 49, then decreased with a rate of 13.5 until 67 and decelerated to a rate of 6.6 per year (Figure 3h).

IV. DISCUSSION

In our study, women showed an accelerated reduction of vBMD during the menopausal period while previous studies reported that aBMD only showed a rapid decline in the late perimenopause [8]. This indicates that bone quality declines as early as the beginning of the menopause transition even when overall bone density appears normal [9]. We observed lower vBMD in Vietnamese women compared to that of their Japanese, Scottish, and German counterparts at the radius. Similar studies indicate that Japanese women have higher vBMD than other Asians populations [10]. Vietnamese men had similar cortical thickness and density to Australian men. They generally had higher cortical thickness than women, peaking around age 35, similar to Japanese men, who also reach peak thickness in their mid-thirties, followed by a decline [11]. The polar stress-strain index, reflecting bone strength, was higher in men in this study and others, attributed to a larger cortical cross-sectional area and thicker cortices [12]. The present results should be interpreted, considering both strengths and potential limitations. This study uses data from a large population-based osteoporosis study in Asian populations, primarily recruiting participants from Ho Chi Minh City, which includes a geographically diverse urban population. The study follows Clinical & Laboratory Standards Institute criteria to ensure a representative sample, though rural populations may be underrepresented. Its cross-sectional design limits the ability to assess longitudinal changes or causal relationships.

V. CONCLUSION

In conclusion, these data have provided a normative reference value for pQCT bone parameters in the Vietnamese population in both genders, which can help clinicians, researchers, and the public interpret bone quality data for individual patients.

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