Estimated Volumetric Bone Mineral Density in a Rural Thai Men and Women: Khon Kaen Osteoporosis Study (KKOS)

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The authors examined the areal bone mineral density (aFNBMD) and estimated volumetric bone mineral density at the femoral neck (vFNBMD) in rural Thai men and women. A total of 181 men and 255 women, between 20 and 84 years of age, living in rural areas of Khon Kaen province, were randomly selected. Areal FNBMD and estimated v FNBMD were determined using dual energy X-ray absorptiometry (DPX-IQ, GE Lunar Corp, Madison, WI). Men had a significantly higher aFNBMD than women, whereas the estimated vFNBMD was similar regardless of sex. The peak for the aFNBMD vs. vFNBMD was observed between 20 and 29 vs. 30 and 39 years of age in men and women, respectively. The prevalence of osteoporosis in men and women using estimated vFNBMD vs. aFNBMD cut-offs was 19 and 14.2 vs 11.8 and 26 percent, respectively. Prevalence increased with age. Estimated vFNBMD shows only small sex-correlated differences in bone density. Estimated vFNBMD was more sensitive than aFNBMD, when used to define the osteoporotic cut-offs in men, while it was less sensitive than aFNBMD in women.

Keywords: *Osteoporosis, Bone mineral density, Asians, Epidemiology*

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Bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) is a primary predictor of osteoporotic fracture and, therefore, a surrogate measure of osteoporosis[1]. Areal bone mineral density (aBMD) is a measure relative to a two-dimensional cross-sectional area (g/cm^2), while volumetric bone mineral density (vBMD) is a measure of bone mass, related to the three-dimensional bone volume (g/cm^3). Since aBMD is influenced by sex, body size, geometry, quality and composition[2-7], using vBMD may more accurately reflect bone density[8]. There is a scarcity of data on which to base an examination of vBMD, particularly among Asians. The present study was designed to investigate the aBMD and estimated-vBMD among adult, rural, Thai adults.

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Material and Method

Setting and Subjects

The authors conducted a cross-sectional investigation in the Muang (central administrative) district of Khon Kaen province, Thailand, where a large proportion of the population is rural-based farmers. Subjects were recruited from two villages (each comprising 14 hamlets) in Muang district. A complete list of potential subjects was obtained from each hamlet and subjects were selected at random and asked to participate. Those with bone disorders, chronic diseases or a history of taking medications affecting calcium and bone metabolism (*i.e.* steroids or thyroid hormone, fluoride, bisphosphonates and calcitonin) were excluded. The study was approved by the Ethics Committee of Khon Kaen University, and written informed consent was obtained from each participant. The study was conducted in accordance with the 1975 (revised 1983) Helsinki Declaration.

Measurements

Body weight (while wearing light indoor clothing) was measured using an electronic balance scale (accurate to the nearest 0.1 kg) and standing height (without shoes) with a stadiometer (accurate to the nearest 0.1 cm). Body mass index (BMI) was calculated as the ratio of weight (kg) over height squared (m^2).

The areal femoral neck BMD (aFNBMD) (g/cm^2) was measured by DXA using a LUNAR DPX-IQ densitometer (GE Lunar Corp, Madison, WI, USA). At the authors' institution, the coefficient of variation of aBMD for the proximal femur among normal subjects is 1.3%. The aFNBMD is derived from the ratio of the femoral neck bone mineral content (FNBMC) and the projected area of a skeletal region. The product of mass and area is not a true measure of density, which has units of mass and volume.

To obtain an index of volumetric bone density (mass/volume), vFNBMD was calculated by dividing FNBMC by the volume of the skeletal sites of interest[8,9]. While FNBMC was obtained directly from the DXA software output, the volume of the various skeletal regions was mathematically estimated using DXA derived area measurements and the assumption made by the DXA software in determining the regions of interest when scanning.

The average diameter *(d)* of the femoral neck was obtained from LUNAR software that uses a fixed length *(h)* along the femoral neck for the measurement of aBMD and BMC. The area measured, calculated as BMC/aBMD, is equivalent to $h \times d$, and this average neck diameter was used to estimate the cross-sectional area (CSA; $\pi (d/2)^2$). The femoral neck volume (FNVOL) was estimated using methods described by Faulkner *et al*[9]. A cylindrical shape was assumed for the FNVOL and volume was estimated by $\pi (d/2)^2 \times h$. As the projected area of the femoral neck is based on a constant length along the axes of the neck of 1.5 cm *(h)*, it is possible to estimate the vFNBMD at this site, by expressing FNVOL as a function of FNBMC and FNBMD. It can be shown algebraically that $FNVOL = \pi (FNBMC)^2/6 \times (aFNBMD)^2$. The estimated vFNBMD was derived as; $6 \times (aFNBMD)^2/\pi (FNBMC)$ in g/cm^3.

Based on the values for estimated vFNBMD, each subject was classified as "osteoporotic" with a vFNBMD of 2.5 SD or more below the young normal level, or "osteopenia" with a vFNBMD between 2.5 to 1.0 SD below the young normal level, or as "normal".

Statistical analysis

Statistical analyses were performed using SPSS version 9.0 (SPSS, Inc, Chicago). Data analysis was performed separately for men and women. Descriptive results were expressed as means, standard deviations (SD) and per cent. Comparisons between men and women were made using the unpaired *t*-test. Correlations between measures of bone content, age and anthropometric values were obtained using the Pearson correlation coefficient (*r*). Simple linear regression analysis was used to estimate the strength of association between age, weight, height and BMD. Statistical significance was set at $p < 0.05$.

Results

A total of 181 men and 255 women with complete data were included in the analysis. The average age of the men and women was 49 ± 17 and 50 ± 16 years, respectively. The average menopausal age was 49 years. Men were significantly heavier and taller, but had lower BMIs than women. The bone parameters, FNBMC, FNVOL and aFNBMD, were significantly higher in men than in women ($p < 0.001$), but vFNBMD was equivalent (Table 1). In the present study, the peak aFNBMD *vs* vFNBMD was observed between 20 and 29 *vs* 30 and 39 years in men and women, respectively. However, women had significantly higher vFNBMD than men between 30 and 49 years of age, but the difference in vFNBMD after 50 years of age was not statistically significant.

In both men and women, weight was positively associated with all the bone parameters ($r = 0.17$-0.51, $p < 0.001$), whereas age was negatively correlated with all the bone measures ($r = 0.48$-0.67, $p < 0.001$) except for FNVOL and CSA ($r = -0.02$, $p = 0.62$). For men *vs* women (respectively) height was associated with aFNBMD ($r = 0.26$ *vs* 0.29, $p < 0.001$), FNBMC ($r = 0.26$ *vs* 0.38, $p < 0.001$), vFNBMD ($r = 0.17$, $p = 0.03$ *vs* $r = 0.14$, $p = 0.02$); however, it was correlated with FNVOL and CSA in women ($r = 0.34$, $p < 0.001$) but not in men ($r = 0.12$, $p = 0.11$). The correlation between aFNBMD and vFNBMD in men and women was 0.90 and 0.94 ($p < 0.001$), respectively.

The authors observed aFNBMD and vFNBMD decreased with advancing age in both men and women (Fig. 1). Based on the peak vFNBMD for the entire population derived from young adults (mean ± SD: 0.46 ± 0.06 for men and 0.46 ± 0.07 for women) (Table 2), the prevalence of osteoporosis was 19.0 and 14.2 per cent, respectively. When using aFNBMD, the prevalence was 11.8 and 26 per cent, respectively. The prevalence in men and women increased with advancing years: in individuals over 50

years, the prevalence using estimated vFNBMD was 33.3 and 24.3 per cent, respectively. By comparison, when using aFNBMD, the prevalence in men and women was 23.3 and 46.3 per cent, respectively. Using aFNBMD and estimated vFNBMD, 95 and 89 percent, respectively, of osteoporosis was found in subjects 50 years and over.

In the unadjusted analysis, age, weight and height were each associated with aFNBMD and estimated vFNBMD in both men and women. However, when the three factors were entered simultaneously, only age and weight were significantly associated with aFNBMD and estimated vFNBMD in both sexes. In men *vs* women, each one-year increase in age was associated with a 6.21 *vs* 8.14 mg/cm^2 decrease in aFNBMD; and a 2.53 *vs* 3.60 mg/cm^3 decrease in estimated vFNBMD, respectively. Furthermore, each one-kilogram increase in weight in men and women was associated with a 4.75 *vs* 5.78 mg/cm^2 increase in aFNBMD and a 0.95 *vs* 1.58 mg/cm^3 increase in estimated vFNBMD, respectively. Age and weight had a more pronounced affect on aFNBMD than estimated vFNBMD in both men and women, but more so in women (Table 3).

Discussion

Osteoporosis is increasingly recognized as a public health concern the world over[1,10,11]. It is gener-

Table 1. Characteristics of study subjects

Variables	Men (n=181)	Women (n=255)	Mean difference (95% CI)
Age (yr)	49.1±17.1	50.6±15.9	-1.50 (-4.7, 1.6)
Weight (kg)	58.2±8.8	55.9±10.5	2.30 (0.6, 4.2)†
Height (cm)	161.2±5.9	152.1±5.2	9.10 (8.1, 10.1)*
Body mass index (kg/m^2)	22.4±2.8	24.1±4.0	-1.70 (-2.3, -1.1)*
FNBMC (g)	4.76±1.10	3.82±0.92	0.94 (0.74, 1.13)*
FNVOL (cm^3)	12.83±2.72	10.18±1.78	2.65 (2.22, 3.07)*
CSA (cm^2)	8.55±1.80	6.79±1.19	1.76 (1.48, 2.05)*
Areal FNBMD (g/cm^2)	0.96±0.18	0.87±0.19	0.09 (0.06, 0.13)*
Volumetric FNBMD (g/cm^3)	0.37±0.07	0.38±0.08	-0.01 (-0.02, 0.01)

FNBMC; femoral neck bone mineral content
FNVOL; femoral neck volume
CSA; cross-sectional area
FNBMD; femoral neck bone mineral density
*Statistically significant at $p < 0.001$
†Statistically significant at $p < 0.05$

Table 2. Areal FNBMD and volumetric FNBMD in men and women by age group

Age group	Areal FNBMD		Volumetric FNBMD	
	Men	Women	Men	Women
20-29	1.18±0.14	1.01±0.12	0.46±0.06	0.45±0.07
30-39	1.02±0.13	1.05±0.14	0.40±0.06	0.46±0.07
40-49	0.96±0.11	0.95±0.12	0.38±0.05	0.41±0.06
50-59	0.94±0.16	0.87±0.14	0.37±0.06	0.37±0.06
60-69	0.84±0.11	0.73±0.15	0.32±0.04	0.32±0.07
>70	0.83±0.17	0.63±0.10	0.32±0.05	0.28±0.05

FNBMD; femoral neck bone mineral density

Table 3. Regression analysis

		Age (per 1 year)	Weight (per 1 kilogram)	R^2
Men	Areal FNBMD/ Volumetric FNBMD	-6.21 ± 0.59*/-2.53 ± 0.24*	4.75 ± 1.16*/0.95 ± 0.47†	0.67/0.78
Women	Areal FNBMD/ Volumetric FNBMD	-8.14 ± 0.49*/-3.60 ± 0.24*	5.78 ± 0.74*/1.58 ± 0.37*	0.64/0.71

Values are the coefficients ± SE. FNBMD; femoral neck bone mineral density
*Statistically significant at $p < 0.001$
†Statistically significant at $p < 0.05$

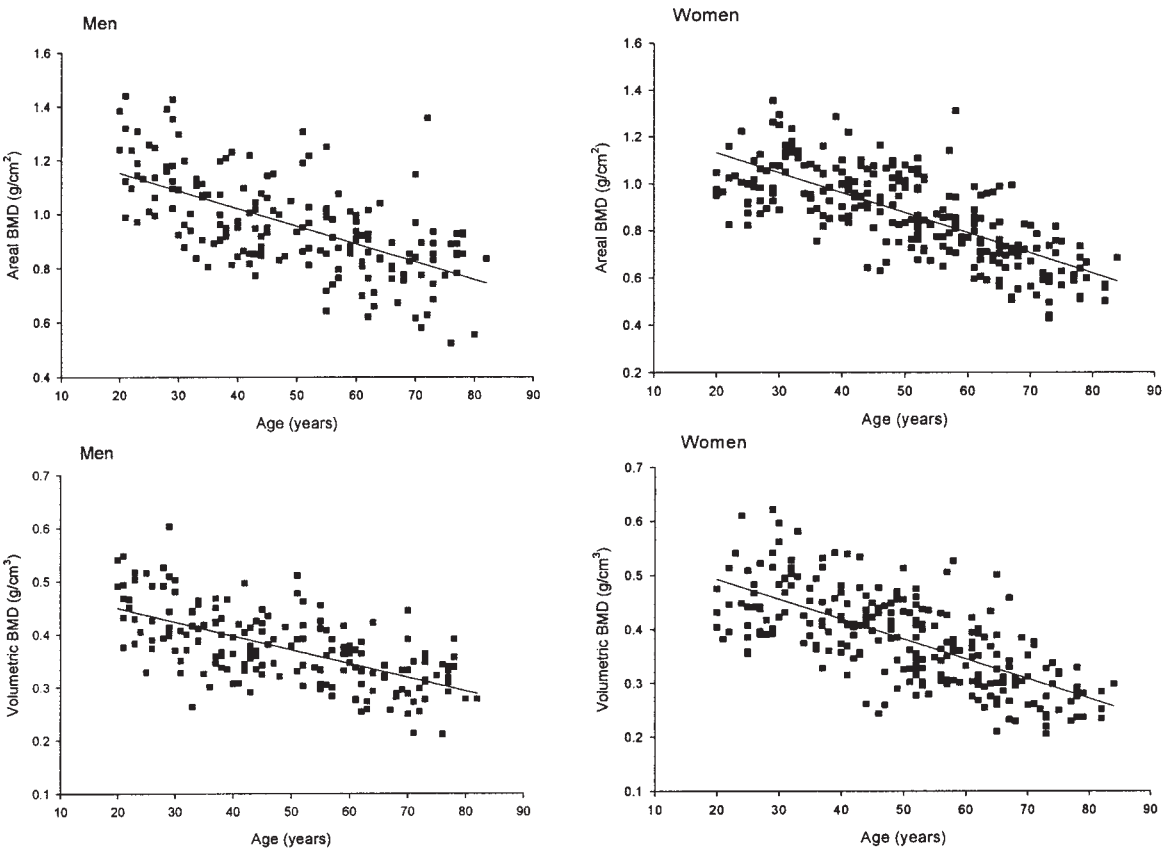

Fig. 1 Age and femoral neck bone mineral density in men and women

ally accepted that aBMD, measured by DXA, is the strongest predictor of osteoporotic fracture(s)[1]. However, more recent studies have found that the relationship is confounded by bone size[3,7,12,13]. Volumetric BMD is a measure of bone mass relative to three-dimensional bone volume (g/cm^3) as opposed to aBMD (g/cm^2), and may be a more accurate reflection of bone density.

The authors found that men had significantly higher FNBMC, FNVOL, CSA and aFNBMD than women; however, the difference in aFNBMD between men and women, using the usual aFNBMD measure, disappeared when an estimate of vFNBMD was used. Moreover, the peak of estimated vFNBMD in the present study was similar in both men and women (0.46 ± 0.06 and 0.46 ± 0.07, respectively), consistent with several previous studies[9,15-18], but not with two others[7,19]. In a larger study, the vBMD was determined from DXA measures in a population-based, age-stratified sample of 350 men and 350 women (between 20 and 29 years of age), mean estimated vFNBMD was significantly higher among women[7].

Most previous studies have found that the risk of fracture in women is 2- to 3-fold higher than in men because, it is thought, of a lower aBMD in women than in men[7,20,21]; however, there are a number of factors associated with aBMD that influence fracture risk.

Areal BMD is a two-dimensional representation of a three-dimensional quantity, with the third dimension (depth) being ignored. Therefore, for the same vBMD, a larger bone will have a higher aBMD. Previous studies have demonstrated that larger aBMD in elderly men compared with elderly women is due primarily to their larger bone size[2,12]. In contrast, estimates of vBMD are similar in men and women[15,18]. The larger bone size in men, translates into a larger CSA and confers a biochemical advantage and greater bone strength[13,23,24]. It could then be hypothesized that larger size, rather than any differences in bone density *per se,* would be a major protective factor for men over women.

There is substantial epidemiologic and clinical data supporting the use of BMD (*i.e.* T-score 2.5 SD below the young normal range) in women to identify an individual at a relatively high risk of fracture and in

whom preventive treatment is warranted[10]. Little evidence exists of a similar T-score-based stratification for men[25].

The present study showed that the young, normal reference to identify osteoporosis using aFNBMD was different between men and women, while comparable when using estimated vFNBMD. Indeed, more than 2.5 SD below the young normal cut-off used to define osteoporosis in women was selected by the WHO because it identified a proportion of women comparable to the expected lifetime fracture risk[26] and there have been many epidemiologic studies to support the use of this value[10].

Despite the 2.5 SD cut-off in women identified as those at higher risk, it is clear that a large proportion of the fractures occurred in those with T-scores above the 2.5 SD threshold[27]. The optimal cut-off value in men is an even more contentious issue as it is still debated whether it should be based upon the young female or male normal values[25,28,29]. This problem lies not in the relative scarcity of data in men but also in the size-effect of the aBMD measure. Notwithstanding, the present data suggest that the young normal reference using estimated vFNBMD in men and women was nearly equivalent.

It is generally accepted that one of the reasons women have a higher incidence of osteoporotic fractures[30] is because women have 'weaker' bones than men. This axiom is based on the finding that the aBMD is lower in women than men of a similar age[21,31]. It has been suggested that women lose relatively more bone mass with age than men[32,33]. These conclusions are based largely on data that has been collected using single/dual photon or X-ray absorptiometry. However, the software in these instruments calculates bone mass (the amount of bone in a three-dimensional "block of bone") relative to a two-dimensional cross-sectional area (aBMD in g/cm^2)[9]. When comparing the aBMD values of men and women, the smaller skeletons of women can lead to false conclusions.

Sex vis-à-vis bone size is a potential confounder when using the areal-density projection method and the present study confirmed this. A comparison of vBMD in men and women demonstrated only small differences in bone density between sexes. Lower bone mass in women compared to men is due more to a smaller bone size than greater differences in densities. Variation in the bone size rather than differences in bone density contributes to the lower skeletal mass in women. Therefore, bone size may be an important factor in explaining the higher age-specific incidence of osteoporotic fractures in women. As has been suggested [14,34], the pathogenesis of bone fracture is heterogeneous. Bone size and bone quality, together with factors related to the external forces imparted at different skeletal sites, are likely important.

The present study had a number of advantages but also some limitations. Firstly, this was a cross-sectional study, which did not allow for the establishment of cause and effect. Secondly, the estimation of vFNBMD using DXA measurements provided only a partial correction of bone size, despite such estimates having been highly correlated with volumetric quantitative CT measurements of BMD[35]. Thirdly, the present data relate only to an estimate of volumetric bone density at the femoral neck, and thus similar conclusions cannot be drawn regarding estimates of vBMD at the lumbar spine. However, femoral neck BMD is subject to less degenerative artifacts than spinal BMD and is generally regarded as a better single measure for prediction of hip fracture[36]. Nevertheless, the present study had the advantage of being based on large, random sampling of rural Thais.

The authors conclude that volumetric BMD at the femoral neck in healthy rural men and women shows only small differences in bone density between the sexes, and that estimated volumetric BMD is more sensitive than areal BMD when used to define an osteoporotic cut-off for men, but less sensitive than areal BMD in women.

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การศึกษาความหนาแน่นของกระดูกชนิดวอลลูมเมตริกในคนไทยที่อาศัยอยู่ในเขตชนบท จังหวัดขอนแก่น

ฉัตรเลิศ พงษ์ไชยกุล , ทวน เหงี่ยน., ชิงชิง ฟู่เจริญ, รัชตะ รัชตะนาวิน

ได้ทำการศึกษาความหนาแน่นของกระดูกชนิดเอเรียลและวอลลูมเมตริกที่ตำแหน่งกระดูกสะโพกในคนไทยที่อาศัยอยู่ในเขตชนบท จังหวัดขอนแก่น มีอาสาสมัครเข้าร่วมวิจัยเป็นเพศชายจำนวน 181 คนและเพศหญิงจำนวน 255 คน อายุระหว่าง 20-84 ปี ทำการวัดความหนาแน่นของกระดูกด้วยเครื่องวัดความหนาแน่นของกระดูก (Lunar DPX-IQ) ผลการศึกษาพบว่าเพศชายมีความหนาแน่นของกระดูกชนิดเอเรียลสูงกว่าเพศหญิงอย่างมีนัยสำคัญทางสถิติ ในขณะที่ไม่พบความแตกต่างของความหนาแน่นของกระดูกชนิดวอลลูมเมตริกระหว่างสองเพศ มวลกระดูกสูงสุดทั้งความหนาแน่นของกระดูกชนิดเอเรียลและวอลลูมเมตริกในเพศชายอยู่ระหว่างอายุ 20-29 ปีในขณะที่เพศหญิงอยู่ระหว่าง 30-39 ปี ความชุกของโรคกระดูกพรุนเมื่อใช้ความหนาแน่นของกระดูกชนิดวอลลูมเมตริกในเพศชายและหญิงพบร้อยละ 19 และ 14.2 ตามลำดับ ในขณะที่ความชุกของโรคกระดูกพรุนเมื่อใช้ความหนาแน่นของกระดูกชนิดเอเรียลในเพศชายและหญิงพบร้อยละ 11.8 และ 26 ตามลำดับ โดยพบความชุกของโรคเพิ่มขึ้นตามอายุ โดยสรุปจากการศึกษานี้พบว่าความหนาแน่นของกระดูกชนิดวอลลูมเมตริกมีความแตกต่างกันเล็กน้อยระหว่างเพศชายและหญิง โดยในเพศชายพบว่าการใช้ความหนาแน่นของกระดูกชนิดวอลลูมเมตริกจะมีความไวมากกว่าการใช้ความหนาแน่นของกระดูกชนิดเอเรียลในการวินิจฉัยโรคกระดูกพรุน ในขณะที่ในเพศหญิงการ ใช้ความหนาแน่นของกระดูกชนิดเอเรียลจะมีความไวมากกว่าการใช้ความหนาแน่นของกระดูกชนิดวอลลูมเมตริก