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Relationship of age-related concentrations of serum FSH and LH with bone mineral density, prevalence of osteoporosis in native Chinese women

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ABSTRACT

Background: Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) may play an important role in bone mass regulation in postmenopausal women.
Methods: A cross-sectional study of 699 healthy Chinese women, aged 20 to 82 y, was conducted. Serum FSH and LH and BMD were measured at the posteroanterior (PA) spine, lateral spine, total hip, and distal forearm.
Results: The geometric mean values (±SD) of serum FSH and LH in premenopausal women were 3.94±2.08 and 7.51±2.58 IU/l, respectively, and in postmenopausal women were 28.8±1.88 and 25.6±1.95 IU/l, respectively. The correlation of FSH to BMD at different skeletal regions ($r=-0.597--0.492$, $P=0.000$) was higher than that of LH to BMD ($r=-0.452--0.332$, $P=0.000$). The prevalences of osteoporosis for the quartiles of FSH at various skeletal sites were 0.57%, 0.43%, 27.1%, and 30.9%, respectively; and of LH were 2.14%, 4.43%, 19.5%, and 26.0%, respectively. The prevalence of osteoporosis in 3rd and 4th quartile was more significantly increased than the 1st and 2nd quartile.
Conclusions: These data suggest that FSH and LH levels in circulation are associated with BMD changes and osteoporosis occurrence in Chinese women.

1. Introduction

Osteoporosis is now recognized as a "silent epidemic disorder" [1] that affects an estimated 75 million people in Europe, the U.S., and Japan [2]. In China, about 88 million patients suffer from this disease [3]. The prevalence of osteoporosis is estimated to be 49% among women >50 y in Japan [4]. There are nearly 45 million women worldwide with fracture affected by osteoporosis that far exceed the combined incidences of breast cancer, stroke and heart attacks [5,6]. Thus, osteoporosis is recognized as a major public health problem in both developed and developing countries alike.

Most research to date attributes postmenopausal osteoporosis or bone loss after female gonadectomy to estrogen deficiency [7–9]. New research challenges this view by demonstrating that FSH directly regulates bone mass by stimulating osteoclastic bone resorption through the tumor necrosis factor-α (TNF-α) [6]. No correlation between FSH-caused osteoclastic bone resorption and estradiol levels has been shown [10]. In vivo studies suggest that BMD decreases significantly during amenorrhea along with increased FSH levels [11,12]; thus, serum FSH levels were significantly negatively associated with BMD [11,13] and were positively associated with bone turnover markers [13]. BMD significantly decreased in postmenopausal women with elevated serum FSH levels [14]. Serum FSH levels were higher and BMD loss was larger during menopause transition; therefore, changes of serum FSH predicting bone loss preceded changes of estradiol and testosterone [15], and BMD was not associated with serum estradiol, testosterone, and sex hormone binding globulin (SHBG) [16]. Studies also found that serum FSH increases and inhibins decreases were related to bone loss in perimenopausal women [17,18], and serum FSH and LH were the major predictors of BMD changes in men [19]. These data sufficiently indicate that FSH and LH may be the direct regulators of bone mass. Studies have also found differences of serum FSH in different ethnic female [20,21]. To investigate the relationship between age-related concentrations of serum FSH and LH with both BMD and the prevalence and risk of osteoporosis in native Chinese women, we conducted a cross-sectional study on 699 healthy Chinese women aged 20 to 82 y to measure serum FSH and LH concentrations and BMD at the PA spine, lateral spine, total hip, and ultradistal forearm and evaluated the relationship between them.

Abbreviations: FSH, follicle-stimulating hormone; LH, luteinizing hormone; BMD, bone mineral density; PA, posteroanterior; SHBG, sex hormone binding globulin; IU, international unit; TNF, tumor necrosis factor; RIA, radioimmunoassay; DXA, dual-energy X-ray absorptiometry; RUUD, radius+ulna ultradistal; RMSCV, root-mean-square coefficient of variation; GnRH, gonadotropin-releasing hormone; BMC, bone mineral content; RANKL, receptor activator of the NF-κB ligand; Lat, lateral; AM, age at menopause; YSM, years since menopause.

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2. Subjects and methods

2.1. Study subjects

A total of 699 healthy Chinese women, aged 20–82 y (mean ± SD, 45.2 ± 14.6 y), were randomly selected between June 2005 and September 2007. These volunteers, all residents of Changsha and surrounding regions, were recruited by public health organizations (i.e., health stations/clinics) providing health care for local residents. All subjects were screened using a detailed questionnaire, history, and physical examination. Subjects were excluded from the study if they had conditions affecting bone metabolism, such as diseases of kidney, liver, parathyoid, thyoid, diabetes mellitus, oligomenorrhea or menopause <40 y, hyperprolactinemia, oopherectomy, rheumatoid arthritis, ankylosing spondylitis, malabsorption syndromes, malignant tumors, hematologic diseases, or previous pathological fractures. Subjects were also excluded if they had been receiving glucocorticoids, estrogens, thyoid hormone, fluoride, bisphosphonate, calcitonin, thiazide diuretics, barbiturates, antiseizure medications, vitamin D or calcium-containing drugs, and habits of smoking, alcohol and caffeine consumption. The study involved a total of 464 premenopausal women and 235 postmenopausal women (last menses >12 months before the study started); of the latter, the mean age at menopause was 48.3 ± 3.84 y (range 41–59 y), and the median duration of menopause was 11.2 years (range 1–42 y). The study was approved of the Ethical Committee of Xiang-Ya Medical College, Central South University (China) and all participants provided written consent to participate.

2.2. Laboratory methods

Fasting morning (7–9 am) blood samples were collected and centrifuged within 1 h and stored at −70 °C until measurements were performed. Blood samples were collected from premenopausal women between days 5 and 9 of the menstrual cycle. A single blood sample was obtained from postmenopausal women on any convenient day. We measured serum FSH and LH concentrations with a radioimmunoassay (RIA) kit (Biotechnology Institute of the North, Beijing, China), respectively, and using a XH-6020 model γ counter (262 Factory, Xian, China). The lower detection limit for serum FSH was 0.20 IU/l and the intra-assay and inter-assay CVs were, respectively, 6.3% and 10.8%. The lower detection limit for serum LH was 0.20 IU/l, and the intra-assay and inter-assay CVs were 7.1% and 11.4%, respectively.

2.3. Bone densitometry

BMD was measured using a dual-energy X-ray absorptiometry (DXA) fan-beam bone densitometer (Hologic Delphi A; Hologic, Bedford, MA) at the supine lumbar spine, including the posteroanterior (PA) spine vertebrae L1–L4, followed by a paired PA/lateral spine scan of the vertebral bodies of L2–L4; at the left hip; and at the radius+ulna ultradistal (RUUD) of the nondominant forearm. The in vivo precision deviations in 33 subjects of 2 repeated BMD measurements that was determined by the root-mean-square coefficient of variation (RMSCV) method [22] were 0.86% for the PA spine, 2.06% for the lateral spine, 0.83% for the total hip, and 1.35% for RUUD. The control spine phantom scan performed on each day demonstrated long-term (>11 y) CVs of <0.44%.

2.4. Statistical analysis

All calculations were performed using SPSS V13.0 for Windows software (SPSS Inc., Chicago, IL). The geometrical mean and SD were used for FSH and LH, as they followed a logarithmic normal distribution. All subjects were stratified by 10-y age and quartile of the FSH and LH groups, respectively, and the FSH and LH concentrations reported as the mean and SD in each group. The mean values of different parameters from different groups were compared with each other for significant differences and assessed using one-way ANOVA whenever significant. The serum FSH and LH concentrations change with age were evaluated and the best-fitting models were determined with the largest R^2 from a comparison of the various regression models, including linear, logarithmic, inverse, quadratic, cubic, compound, power, growth, exponential, S, and logistic equations. According to the World Health Organization (WHO) definition [23] and the bone mineral density reference databases established by our group [24], subjects with BMD of 2.5 SD lower than the peak mean of the sane gender (*T*-score ≤ −2.5) were determined to be osteoporotic. The χ^2 test was utilized to compare the prevalence of osteoporosis in different quartile groups.

Table 1
Distribution by number, height, weight and body mass index (BMI) in different age groups

Age (y)	*n*	Height (cm)	Weight (kg)	BMI (kg/m^2)
20–29	129	157.6±5.56	50.0±6.49	20.1±2.33
30–39	138	156.6±5.20	53.9±7.40	22.0±2.50
40–49	154	155.1±5.06	56.8±7.76	23.6±2.91
50–59	133	152.8±4.51	55.2±8.93	23.6±3.50
60–69	124	151.1±4.82	54.1±8.57	23.7±3.25
≥70	21	151.5±3.88	54.2±8.27	23.6±3.48
All	699	154.6±5.52	54.1±8.15	22.7±3.23

Note. Values are mean (±SD).

Table 2
Correlations (*r*) between gonadotrophins and age, age at menopause (AM), years since menopause (YSM), height, weight, and body mass index (BMI) in Chinese females

	Follicle-stimulating hormone		Luteinizing hormone	
	Coefficient (*r*)	*P*-value	Coefficient (*r*)	*P*-value
Age	0.636	0.000	0.457	0.000
AM	−0.121	0.042	0.043	NS
YSM	−0.172	0.003	−0.389	0.000
Height	−0.377	0.000	−0.283	0.000
Weight	−0.067	NS	−0.070	NS
BMI	0.115	0.003	0.065	NS

Note. NS, no significance.

3. Results

3.1. Subject characteristics and correlation with FSH and LH

Table 1 shows the age-dependent distribution of the subjects by number, height, weight, and body mass index (BMI). Subject height decreases with increases in age. Weight and BMI increase with age <50 y. Weight peaks between 40 and 59 y and BMI remains constant after 40 y. Table 2 demonstrates the correlation between FSH and LH concentrations and age, menopausal age, years since menopause, and anthropometry indexes. In females, age significantly positively correlates with serum FSH and LH concentrations, while FSH and LH concentrations negatively correlate with years since menopause and subject height. Serum FSH concentration positively correlates with BMI.

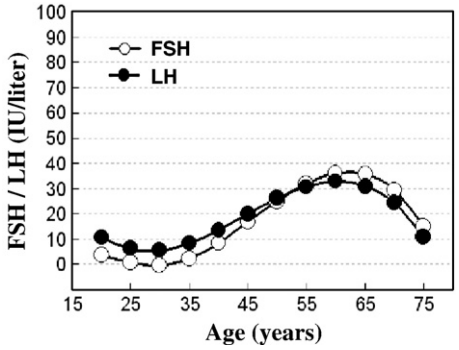

Fig. 1. Comparison of curve-fitting models of age-related changes in serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels in Chinese women. Cubic regression equation: FSH = 139.097 − 11.364 (age) + 0.286 (age)^2 − 0.002 (age)^3; LH = 106.002 − 8.459 (age) + 0.220 (age)^2 − 0.002 (age)^3.

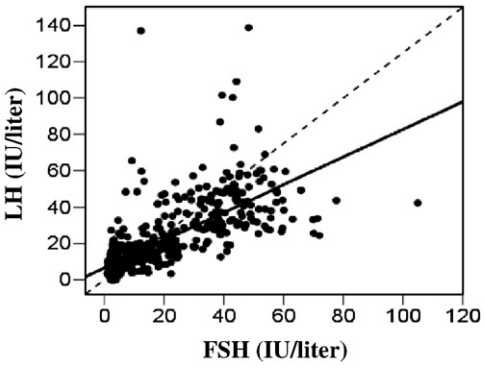

Fig. 2. Correlation scatter diagram of serum follicle-stimulating hormone (FSH) with luteinizing hormone (LH) concentrations in healthy Chinese women. $y = 6.566 + 0.762x$, $r = 0.734$ ($P = 0.000$), $n = 699$.