

Stiffness Index of the Calcaneus Measured by Quantitative Ultrasound and Menopause among Japanese Women: The Hizen-Oshima Study

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Department of Public Health, Nagasaki University School of Medicine, Nagasaki 852-8523, ¹Department of Orthopedic Surgery, Nagasaki University School of Medicine, Nagasaki 852-8501, ²Nagasaki University School of Health Sciences, Nagasaki 852-8520, and ³Department of School Health, Faculty of Education, Nagasaki University, Nagasaki 852-8521

YOSHIMI, I., AOYAGI, K., OKANO, K., YAHATA, Y., KUSANO, Y., MOJI, K., TAHARA, Y. and TAKEMOTO, T. *Stiffness Index of the Calcaneus Measured by Quantitative Ultrasound and Menopause among Japanese Women: The Hizen-Oshima Study*. Tohoku J. Exp. Med., 2001, **195** (2), 93-99 — Quantitative ultrasound (QUS) is a recently developed technique for evaluating fracture risk that can assess both bone mass and architecture. Although numerous studies have shown that menopause is associated with accelerated loss of bone mineral density, there are only a few studies on the association of QUS parameter (stiffness index) with menopausal status, especially among Japanese population. We examined age-specific changes in stiffness index, and relation with age, body mass index (BMI) and menopausal status among 506 community-dwelling Japanese women aged 40-89 years. Mean age at menopause (standard deviation) among 459 women with natural menopause was 49.4 (4.0) years. Stiffness index significantly decreased with increasing age. Stiffness index among 80-89 years age group was 40% lower, compared with that of 40-49 years age group. The greatest decline among adjacent ten-year age groups in stiffness index (15%) was found between 40-49 and 50-59 years of age. Multiple regression analysis showed that menopause related with decreased stiffness index, independent of age and BMI. Our findings indicate that menopause influences loss of bone mass and induces deterioration of bone trabecular microstructure. ——— quantitative ultrasound; menopause; bone mass; osteoporosis
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With increased longevity, the elderly constitute a growing segment of the community. Osteoporosis (low bone mass or density) is one of the most prevalent chronic health problems among the elderly (Cummings et al. 1985; Ross 1996). Since fractures due to osteoporosis lead to considerable disability and many premature deaths, osteoporosis and osteoporotic fractures are major public health concerns (Cummings et al. 1985).

Quantitative ultrasound (QUS) is a recently developed promising technique for evaluation of fracture risk. In addition to the features of portability, ease of use, and relatively low cost, it is also free from ionizing radiation and may provide information on bone structure (Genant et al. 1996).

Numerous studies have shown that estrogen deficiency due to menopause results in accelerated loss of bone mineral density (Lindsay et al. 1978; Horsman et al. 1979; Rigotti et al. 1984; Marcus et al. 1985; Elders et al. 1988; Nilas and Christiansen 1988; Prior et al. 1990). However, there are a few studies on the association of QUS parameter with menopausal status, especially among Japanese population (Yamaguchi et al. 2000; Fukuharu et al. 2001). In evidence-based medicine, the current status of knowledge on a topic is usually determined by the pattern of results of many studies investigating the topic, rather than by one definitive study (Fletcher et al. 1996). Thus, we believe that it is informative to analyze the relation between QUS parameter and menopausal status. In the present study, we examined age-specific changes in QUS, and the relation with age, body mass and menopausal status among community-dwelling Japanese women aged 40 years and over.

SUBJECTS AND METHODS

The Hizen-Oshima Study is a prospective population-based cohort study of musculoskeletal conditions (e.g., osteoporosis and osteoarthritis). We recruited community-

dwelling women aged 40 years and over living in Oshima town, Nagasaki prefecture, Japan. The target group was identified by the municipal electoral list and contacted through mailings. The town of Oshima has a population of approximately 5800, in which the total number of women aged 40 and over is approximately 2000. All women aged 40 and over were invited to participate in the study. Baseline examination was performed at the Oshima Health Center between 1998 and 1999. A total of 586 women (approximately 30% of eligible women) participated in the study. We compared the age distribution of participants vs. non-participants. In total, the mean age of participants (63.9 years) was significantly higher than that of non-participants (61.1 years). Despite having a shipyard in the town, Oshima is mainly a rural (farming/fishery) district. Approximately half of the women who participated in the study continue to grow rice and vegetables by manual labor, though sometimes using machinery. At study entry, all participants were noninstitutionalized and lived independently. All subjects gave written informed consent before examination.

Body weight (kg) and height (m) were measured with the subject in light clothing and without shoes, and body mass index (BMI) was calculated as weight (kg)/height² (m²). QUS of the right calcaneal bone was determined by measurement of broadband ultrasound attenuation (BUA) and the speed of sound (SOS) using the Achilles ultrasound bone densitometer (Lunar Corp., Madison, WI, USA). Stiffness index, a function of BUA and SOS measurements, was calculated using the equation provided by the manufacturer. Preliminary studies indicated that the reproducibility, expressed as coefficient of variation, measured on 5 occasions consecutively within 1 hour, was 1.71% for stiffness index calculated in 17 healthy volunteers. Menopausal status (menopause naturally, menopause artificially or in menstruation) was obtained by question-

naire.

Statistical analysis

Data were expressed as mean (standard deviation). Data were analyzed using the Statistical Analysis System Version 6.12. (SAS Institute Inc., Cary, NC, USA). Stiffness index values were missing for 13 women, menopausal status was missing for 3 women, and menopause was induced artificially in 64 women (including hysterectomy). The above cases were deleted, leaving data of 506 women for analysis. Age-specific means of body weight, height, BMI and stiffness index were computed using general linear modeling method (ANOVA). Multiple linear regression analysis was used to explore the effects of age, BMI and menopausal status on stiffness index, BUA or SOS. Regression models were fit separately for stiffness index, BUA and SOS as dependent variables and age, BMI and menopausal status as independent variables.

RESULTS

Mean age of the subjects was 64.7 (9.8) years (range: 40–89). Four hundred and fifty-nine women (90.7%) were naturally menopausal, and 47 women (9.3%) were in menstruation. Mean age at menopause (standard deviation) among 459 women who had natural menopause was 49.4 (4.0) years.

Both height and weight decreased significantly with increasing age (Table 1).

TABLE 1. Mean (standard deviations) values of height, weight and body mass index (BMI) by age group

Age group (years)	<i>n</i>	Height (cm)	Weight (kg)	BMI (kg/m ²)
40–49	40	155.4 (4.8)	54.6 (7.7)	22.6 (2.8)
50–59	94	153.5 (6.1)	55.3 (9.7)	23.4 (3.8)
60–69	195	149.6 (5.2)	52.4 (8.6)	23.3 (3.4)
70–79	149	146.9 (4.9)	50.7 (8.2)	23.5 (3.4)
80–89	28	141.9 (5.5)	45.0 (6.0)	22.4 (2.9)
<i>p</i> for trend		0.0001	0.0001	0.36

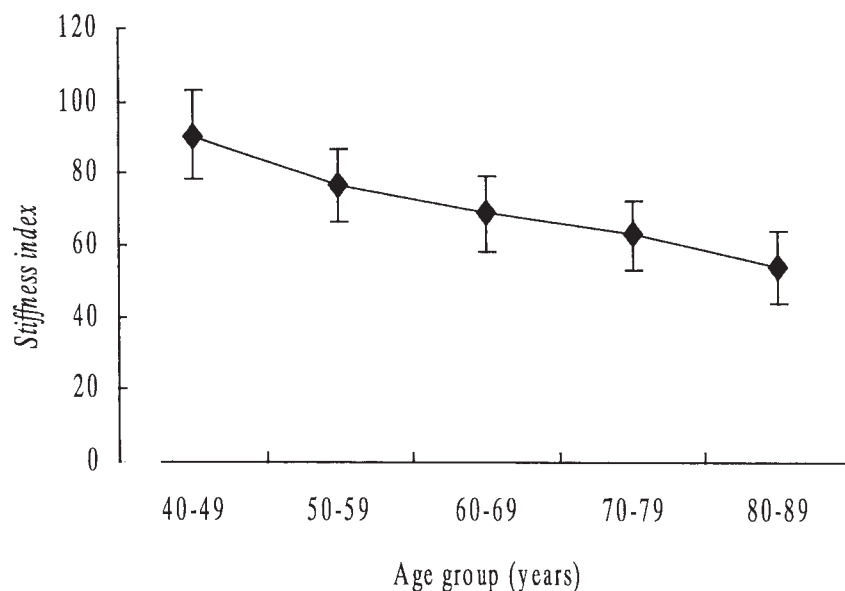


Fig. 1. Stiffness index by age group. Vertical bars indicate standard deviations. Stiffness index decreased significantly with increasing age (p for trend, <0.0001). The greatest decline of stiffness index among adjacent ten-year age groups was found between 40–49 and 50–59 year age groups.

TABLE 2. *Multiple regression model for stiffness index ($R^2 = 0.452$)*

	Coefficient	Standard error	<i>p</i> -value
Intercept	111.64	4.24	0.0001
Age (years)	-0.79	0.06	0.0001
BMI ^a (kg/m ²)	0.61	0.13	0.0001
Menopause ^b	-5.53	1.90	0.0038

^abody mass index.

^bnominal variable of 1 (yes) or 0 (no).

The height and weight among ages 80–89 were 9% and 17% lower than those of 40–49 year age group, respectively. BMI was not different among age groups.

The changes of stiffness index by age group are shown in Fig. 1. Stiffness index decreased significantly with increasing age. Stiffness index among ages 80–89 was 40% lower than that of 40–49 year age group. The greatest decline of stiffness index (15%) among adjacent ten-year age groups was found between 40–49 and 50–59 year age groups.

Multiple regression analysis showed that age, BMI and menopause related significantly with the stiffness index (Table 2); increasing age was associated with decreased stiffness index and higher BMI was associated with increased stiffness index. Menopause was associated with decreased stiffness index, independent of age and BMI. This finding was unchanged when the analysis was repeated using years since menopause instead of menopause (yes/no) in the model (data not shown). In addition, we examined the associations of BUA or SOS with age, BMI and menopause. Age, BMI and menopause related significantly with the BUA, while age and menopause related with SOS (data not shown).

DISCUSSION

QUS is a simple, inexpensive and non-invasive measure of bone density, and has been used in research settings for the prediction of

osteoporosis (Gregg et al. 1997). Although the values measured by QUS moderately correlate with bone mineral density, QUS appears to be as strong a predictor of osteoporotic fracture as direct measurement of bone mineral density and could accurately predict bone fracture independent of bone mineral density (Gregg et al. 1997). Since the pathophysiology of osteoporosis is known to include both a loss of bone mass and alteration of trabecular microstructure (Kleerekoper et al. 1985), it has been suggested that clinical QUS assessment of both bone mass and architecture could improve prediction of fractures (Gregg et al. 1997).

Our results showed that menopause was associated with decreased stiffness index, independent of age and BMI. Numerous studies have shown that estrogen deficiency due to menopause results in accelerated loss of bone mineral density (Lindsay et al. 1978; Horsman et al. 1979; Rigotti et al. 1984; Marcus et al. 1985; Elders et al. 1988; Nilas and Christiansen 1988; Prior et al. 1990). A recent study using QUS showed that menopausal status was associated with lower stiffness index, independent of age, BMI and exercise (Yamaguchi et al. 2000). Furthermore, two recent studies demonstrated that time after menopause was associated with lower stiffness index, independent of age and BMI (Heldan de Moura Castro et al. 2000; Fukuharu et al. 2001).

Stiffness index was calculated in the present study as a function of BUA and SOS measurements. Multiple regression analysis showed that age, BMI and menopause related significantly with the BUA, while age and menopause related with SOS (no association of BMI with SOS). However, Yamaguchi et al. (2000) reported that age, BMI and menopausal status were independently associated with stiffness index, BUA and SOS. The reason for the discrepancy of the association between BMI and SOS is unclear. Further studies are needed to clarify the associations between BMI and SOS.

Our results also showed that stiffness index was significantly decreased with increasing age, confirming previous studies (Yamazaki et al. 1994; Haldan de Moura Castro et al. 2000; Fukuharu et al. 2001; Pluskiewicz and Drozdowska 2001). The greatest fall in stiffness index was found between 40–49 and 50–59 years age groups, and the mean age at menopause of our subjects was 49 years. Yamazaki et al. (1994) found the largest reduction in stiffness index in women aged over 45–49 years. In addition to age-related bone loss, menopause-related acceleration of loss in stiffness index appears to occur in peri-menopausal period as in bone mineral density (Gregg et al. 1997).

In the present study, women with high BMI showed higher stiffness index, compared to those with lower BMI. Many studies reported that obesity (greater body weight or BMI) is associated with higher bone mineral density (Ribot et al. 1987; Nishizawa et al. 1991; Albala et al. 1996; Takata et al. 1999; Murillo-Uribe et al. 2000). Like bone mineral density, QUS is believed to be positively associated with body weight and BMI (Gregg et al. 1997). Yamaguchi et al. (2000) reported that greater BMI is a strong predictor of increased stiffness index among women with a mean age of 57 years who attended a screening examination. Fukuharu et al. (2001) reported that BMI was positively associated with stiffness index in post-menopausal women. The protective effect of obesity on bone loss appears to be related both to mechanical factors and to estrogen synthesis in adipose tissue (Ribot et al. 1994). However, since obesity is an important risk factor for cardiovascular disease and diabetes, adequate BMI should be recommended for general health.

We compared height and weight of our subjects with those of women examined in the National Nutrition Survey, Japan (Japanese Ministry of Health and Welfare 1999). Both height and weight decreased significantly with increasing age in the current study. The

results of the National Nutrition Survey also showed that elderly women had lower height and weight. Thus, age-specific mean values of height and weight of our subjects were not different from those of Japanese women at large.

In conclusion, we demonstrated in the present study that stiffness index measured by QUS decreased significantly with increasing age in women, especially in those at perimenopausal period, and that menopause related significantly with stiffness index, independent of age and BMI. Our findings suggest that menopause may influence bone mass and architecture. Lifestyle-related preventative measures (diet and exercise) should be recommended for prevention of osteoporosis. Furthermore, measurement of bone mass or density is important in lean and post-menopausal women for assessment of future fracture risk, because such women appear to be at a greater risk of osteoporosis (Ravn et al. 1999). The QUS could be a useful non-invasive tool for screening of osteoporosis and assessment of future fracture risk.

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