Effects of Aging and Postmenopausal Hypoestrogenism on Skin Elasticity and Bone Mineral Density in Japanese Women

HIROYUKI SUMINO, SHUICHI ICHIKAWA*, MASATOSHI ABE**, YUKIE ENDO**, YOSHIKAZU NAKAJIMA***, TAKASHI MINEGISHI***, OSAMU ISHIKAWA** AND MASAHICO KURABAYASHI

Second Department of Internal Medicine, Gunma University School of Medicine, Maebashi, Gunma 371-8511, Japan
*Cardiovascular Hospital of Central Japan, Hokkitsu-mura, Gunma 377-0061, Japan
**Department of Dermatology, Gunma University School of Medicine, Maebashi, Gunma 371-8511, Japan
***Department of Obstetrics and Gynecology, Gunma University School of Medicine, Maebashi, Gunma 371-8511, Japan

Abstract. Skin collagen content and bone mass decrease with aging. Loss of collagen from the skin might decrease its elasticity. We investigated associations between skin elasticity, bone mineral density (BMD), age, and menopausal hypoestrogenism. Thirty-eight healthy Japanese postmenopausal women were studied (mean age, 55.7 ± 5.9 yr; range, 48 to 71). Skin elasticity was measured using a suction device applied to the dorsal right forearm. BMD values of L2 to 4 vertebral bodies were measured by dual-energy X-ray absorptiometry. Age showed significant negative correlations with both skin elasticity and BMD (r = –0.57, p<0.001 and r = –0.40, p<0.05, respectively). Years since menopause also showed significant negative correlations with both skin elasticity and BMD (r = –0.51, p<0.01 and r = –0.41, p<0.05, respectively). We also found a positive correlation between skin elasticity and BMD in these postmenopausal women (r = 0.44, p<0.01). In conclusion, we demonstrated declining skin elasticity and bone mass in postmenopausal women to possibly be age- and estrogen-related. Additionally, decreased skin elasticity might serve as a predictor of bone loss in postmenopausal women.

Key words: Age, Skin elasticity, Bone, Menopause, Women

COLLAGEN constitutes approximately one-third of total body mass [1]. Skin and bone share similar loose connective tissue, respectively located in the dermis and the organic bone matrix.

Both bone matrix and dermis are composed of more than 70% type I collagen [2]. Skin collagen content and bone mineral density (BMD) share comparable regressive changes during the aging process. Several studies have reported that skin collagen content decreases with age and loss of estrogen [3–6], while loss of skin collagen is associated with number of years following menopause [3, 5–7]. Menopause is also the major risk factor for bone loss [8–10], and bone density shows an age- and estrogen-related decline [3, 6, 11]. Hypoestrogenism might contribute in parallel to loss of skin collagen and bone mass in women, while collagen loss from skin reduces its thickness and elasticity [6, 12]. However, no simultaneously obtained data have been presented to correlate skin elasticity and bone mineral content with aging and menopausal hypoestrogenism.

A new suction device was recently developed to simply, rapidly, and noninvasively quantify skin elasticity in vivo. Clinical applications of these measurements have been reported by several authors [12–17]. In the present study, we simultaneously measured skin elasticity in the forearm and lumbar spine BMD (L2 to 4) in Japanese postmenopausal women to investigate associations of skin elasticity and bone mineral content with one another as well as with age and duration of menopausal hypoestrogenism.
Materials and Methods

Subjects

We studied 38 healthy Japanese postmenopausal women (mean age, 55.7 ± 5.9 yr; range, 48 to 71). Each patient had experienced natural menopause. Menopausal status was confirmed by measuring the serum estradiol (E2) concentration (<20 pg/ml) and the serum FSH concentration (>40 mIU/ml). No subject had received estrogen, corticosteroid, calcium, bisphosphonate, or vitamin D and K supplements before enrollment. None had any contraindications for such treatments. Before enrollment in the study, each individual underwent physical and laboratory examinations including a gynecologic evaluation and mammography, vertebral radiography, 12-lead electrocardiography, and echocardiography. Exclusion criteria were skin disorders such as extensive burns, scars, or psoriasis; actinic keratoses; cutaneous cancer; a past or present history of Cushing syndrome; acromegaly; scleroderma; lupus erythematosus; rheumatoid arthritis; compression fractures; grade 4 osteophytes; diabetes mellitus; thyroid disease; acute or severe chronic liver disease; heart failure; renal failure; thromboembolic disease; ischemic cardiac disease; diastolic blood pressure above 95 mm Hg; unexplained vaginal bleeding; and breast or endometrial cancer. Subjects had indoor occupations and denied having excessive sun exposure. No subject had smoked or used products known to influence epidermal and connective tissue structure, or bone metabolism. Subjects were not allowed to use either emollient or hydrating creams during a 3-day period before evaluation. Written informed consent was obtained from each individual before participation. The study protocol was approved by the Ethics Committee of the Cardiovascular Hospital of Central Japan.

Study protocol

Blood samples were obtained, skin elasticity in the right forearm was tested, and BMD of the lumbar spine (L2-4 BMD) was measured. Skin elasticity in the right forearm was measured noninvasively using a computer-linked suction device equipped with a handheld probe. Blood samples were obtained in the morning after a 12-h fast. Blood was drawn after subjects had been resting in a supine position for at least 10 min.

Measurement of skin elasticity

The equipment used, a Cutometer SEM 474 (Courage and Khazaka Electronic, Koln, Germany), included a microprocessor, an air suction system, and a probe with a vacuum cup 2 mm in diameter. The probe was connected to an electric cable. Air movement in the suction hose was controlled by a personal computer (IBM PC/AT). As in previous reports [12–15], we used three different parameters for analysis: A, A-B, and (A-B)/A. The maximum skin elevation in the vacuum cup after 10 sec at 300 hPa (hecto-Pascal) was defined as A, while the skin elevation 15 sec after release was defined as B (Fig. 1). (A-B)/A represented the ratio of immediate retraction to total deformation. We defined “A” as skin distensibility (extensibility), “A-B” as skin retraction capacity (contractibility), and “(A-B)/A” as skin elasticity.

We made the above measurements on the dorsal aspect of the right forearm, midway between the elbow and the wrist. All measurements were performed by one author (H.S.) to maximize uniformity of measurement conditions, and reproducibility was confirmed by repeated measurements. The intra-assay coefficient of variation (CV) for skin elasticity was 1 to 3%.

Measurement of BMD

BMD of the lumbar spine (L2 to 4) was measured by dual-energy X-ray absorptiometry (DXA; QDR-1000W, Hologic, Waltham, MA, USA) following a conventional procedure as described previously [18–20]. The in vivo and in vitro coefficients of variation

![Fig. 1. Skin deformation plotted as a function of time. A, maximum distension at 300 hPa. B, minimum distension at 0 hPa.](image-url)
of these measurements were less than 0.5%.

Assays

For determinations in plasma, samples of venous blood were placed in polystyrene tubes containing sodium EDTA (1 mg/ml). The EDTA-containing tubes were quickly chilled in an ice bath, and plasma was separated by centrifugation for 10 min at 3100 × g and 4°C. Serum was separated after clot retraction by centrifugation for 10 min at 1000 × g at room temperature. Samples were stored at –80°C until the time of assay. Serum concentrations of FSH and E2 were measured by radioimmunoassay using commercially available kits (Boehringer Mannheim, Germany). Intra- and inter-assay CVs of each method, respectively, were: FSH, 2.0% and 2.9%; E2, 5.0% and 5.6%.

Statistical analysis

Data are presented as means ± SD. Single regression analysis was performed to investigate correlations between age and skin elasticity or BMD, between years since menopause and skin elasticity or BMD, between E2 and skin elasticity or BMD, and between skin elasticity and BMD. Student’s t test was used to analyze differences between the values for age, BMD, and skin elasticity in the high and low BMD groups. A p-value below 0.05 was considered to indicate statistical significance.

Results

Table 1 presents demographic and laboratory characteristics as well as skin and bone assessments in postmenopausal women. Serum FSH and E2 concentrations were consistent with a postmenopausal state.

Correlations were examined for skin elasticity and BMD in postmenopausal women with age (Fig. 2) and with years since menopause (Fig. 3). Age showed significant negative correlations with both skin elasticity and BMD (respectively, r = –0.57, p<0.001 and r = –0.40, p<0.05). Years since menopause also showed significant negative correlations with both skin elasticity and BMD (respectively, r = –0.51, p<0.01 and r = –0.41, p<0.05). Serum E2 showed significant positive correlations with both skin elasticity and BMD (respectively, r = 0.46, p<0.01 and r = 0.36, p<0.05; Fig. 4). We also found a positive correlation between skin elasticity and BMD in postmenopausal women (r = 0.44, p<0.01; Fig. 5).

To exclude effects of age on BMD and skin elasticity,
Subjects were divided into two groups according to BMD values; high BMD group (n = 18) and low BMD group (n = 20). Women with a BMD above 0.885 g/cm² were assigned to the high BMD group, while those with a BMD below 0.885 g/cm² were assigned to the low BMD group. The cut-off point was the mean BMD for all subjects in the study. No significant differences in age were noted between the high and low BMD groups, but BMD and skin elasticity were higher in the former (p<0.001 and p<0.05; Table 2).

Discussion

We demonstrated inverse correlations of skin elasticity and BMD with age and years since menopause in postmenopausal women and positive correlations of serum estradiol with skin elasticity and BMD, and as well as a positive correlation between skin elasticity and BMD.

Age-related skin atrophy was characterized in a previous study [2]. Clinically, aging skin shows fine wrinkling, thinning (reflecting atrophy of the collagenous dermis), and poor wound healing. Examination
of age-related changes in the dermis by light and electron microscopy demonstrated severe disorganization of the elastic fiber network [21] together with a decrease in the number of collagen fiber bundles [22]. One study reported negative correlations between age and skin-fold thickness measured in women using calipers on the dorsum of the hand [23], and another found a negative relationship between age and skin elasticity measured on the forearm with a suction device in normal subjects of both genders [12]. Castelo-Branco et al. [3] described negative correlations of collagen in skin samples taken from the lower abdomen with age and with years since menopause. Brincat et al. [6] demonstrated a negative correlation of years since menopause with collagen content of skin taken from the lower abdomen and lumbar BMD. Chappard et al. [23] found skin-fold thickness on the dorsum of the hand to correlate with vertebral and femoral BMD. Pierard et al. [29] showed a correlation between skin elasticity in the forearm and BMD in the hip and femoral neck. These data are consistent with our present results suggesting a significant correlation between skin elasticity and BMD in postmenopausal women.

The present study has two limitations. First, the number of women enrolled was relatively small. Second, we measured skin elasticity in the right forearm, but did not directly assess dermal collagen content.

Table 2. Comparison of skin elasticity between high and low BMD groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>High BMD group</th>
<th>Low BMD group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Age, yr</td>
<td>54.2 ± 4.6</td>
<td>57.1 ± 6.7</td>
</tr>
<tr>
<td>BMD, g/cm²</td>
<td>0.992 ± 0.087†</td>
<td>0.788 ± 0.062</td>
</tr>
<tr>
<td>Skin elasticity, %</td>
<td>60.8 ± 5.7*</td>
<td>54.2 ± 9.7</td>
</tr>
</tbody>
</table>

Mean ± SD. *p<0.05, †p<0.001 compared with low BMD group (Student’s t test). BMD = bone mineral density.

Mean ± SD. *p<0.05, †p<0.001 compared with low BMD group (Student’s t test).

BMD = bone mineral density.

with our present data. Additional evidence implicating hypoestrogenism in skin collagen loss in menopause is provided by improvement with hormone replacement therapy [4, 5, 17, 24]. Bone mass loss related to menopause also is reversed by such therapy [25, 26]. Thus, hypoestrogenism following menopause is likely to have a profound negative effect on skin elasticity and BMD. Taking these observations together, decrements in skin elasticity and bone mass in postmenopausal women appear to result from hypoestrogenism.

The correlation that we observed between bone and skin elasticity loss suggests a common pathophysiologic mechanism. Parallel skin and bone changes have been observed in several diseases including osteoporosis [27] and anorexia nervosa [28]. Various studies have reported a relationship between postmenopausal skin and bone changes. Castelo-Branco et al. [3] described a correlation between collagen in skin taken from the lower abdomen and lumbar BMD. Chappard et al. [23] found skin-fold thickness on the dorsum of the hand to correlate with vertebral and femoral BMD. Pierard et al. [29] showed a correlation between skin elasticity in the forearm and BMD in the hip and femoral neck. These data are consistent with our present results suggesting a significant correlation between skin elasticity and BMD in postmenopausal women.

The present study has two limitations. First, the number of women enrolled was relatively small. Second, we measured skin elasticity in the right forearm, but did not directly assess dermal collagen content.

In conclusion, we demonstrated declines in skin elasticity and bone mass in postmenopausal women to be age- and estrogen-related, and that loss of skin elasticity might predict bone loss. Decreased skin elasticity is a potential predictor of bone loss in postmenopausal women. Further studies are needed to assess this possibility.

Acknowledgements

We are grateful to Naoaki Tsunoda, Hiroyuki Takada, Hiroe Hagiwara, and Hiromitsu Takahashi for technical assistance. We also thank Kazuo Sakaguchi, Miki Shiroizu, Tomoko Sakurai, Mina Aoki, Yuko Masuda, Kanae Kodaira, Setsuko Kobayashi, Yoshimi Matsuda, and Masumi Tanimoto for assisting with the clinical coordination.
References