Bull Yamaguchi Med Sch 39(3-4) : 37-48, 1992

Quantitative Assessment of Relationships between Abdominal Aortic Calcification and Bone Mineral Content of Lumbar Vertebrae in the Elderly by Computed Tomography

Nobuyuki Sugihara[1], *Masunori Matsuzaki*[1], *Kaneto Furutani*[2], *Yokiko Kato*[3] *and Muneo Miyawaki*[4]

[1] The Second Department of Internal Medicine, Yamaguchi University School of Medicine, Ube, Yamaguchi 755, Japan.
[2] Department of Radiology,
[3] Department of Internal Medicine,
[4] Department of Surgery, Ube First Hospital.
(Received May 25, revised August 10, 1992)

Abstract The relationship between abdominal aortic calcification and osteoporosis in 224 elderly patients (82 men, 142 women, age ranged from 60 to 94 yrs [77.8 ± 7.6]) was investigated by computed tomography. We calculated the aortic calcification index (ACI;%) of calcification volume to aortic volume within 10 slices in the lower abdominal aorta, and measured the bone mineral content (BMC; mg/cm^3) of three lumbar vertebral bodies (the 2nd, 3rd, 4th) using a calibrated phantom. ACI increased, but BMC decreased gradually with aging. ACIs in women were significantly less in the 60s decade of age ($p<0.01$), but higher in the 80s and 90s (NS) than those in men. BMCs in women were significantly less than those in men in the 70s and 80s ($p<0.01$ and $p<0.05$, respectively). In both the 70s and 80s, there were significant negative correlations between ACIs and BMCs in women (70s:$n=61$, $r=-0.371$,$p<0.01$; 80s:$n=55$,$r=-0.334$,$p<0.01$), but was no relation between them in men. These results suggested that in the elderly women, abdominal aortic calcification is closely related to the bone loss caused by postmenopausal osteoporosis.

Key Words : Abdominal aortic calcification, Osteoporosis, Bone mineral content, Atherosclerosis, Computed tomography.

Introduction

The aortic calcification is frequently seen with age or in elderly women, and occurs by the following diseases of hyperlipidemia, diabetes mellitus, hypertension, osteoporosis, renal failure, and hyperparathyroidism [1)-5)]. In the elderly women, an incidence of both osteoporosis and aortic calcification gradually increases, and the relationship between both of them become closely in proportion to aging[6)-8)].

Computed tomography (CT) is the more powerful clinical method to discriminate the calcification from aortic wall than the plain X-ray film or magnetic resonance image[9)-11)]. Recently, CT method also can offer us to establish the qualitative or semi-quantitative measurement for calculating the aortic calcification[4)12)13)]. Similarly, CT method using a calibrated phantom also offers the quantitative measurement of bone mineral content (BMC) in vertebral or femur bone[14)15)]. Therefore, in the present study, we investigated the relationship between the aortic calcification and the osteoporosis in the elderly by a quantitative CT method.

Subjects and Methods

Subjects: The 224 elderly patients of in- and outpatients (82 men, 142 women, age ranged from 60 to 96 years old [mean age 77.8±7.6]) were examined by the CT scanning of abdominal aorta and lumbar vertebrae, simultaneously.

We selected the patients of the following basal diseases: 106 patients with osteoporosis, spondylosis deformans and osteoarthrosis; 87 with cerebrovascular disease; 77 with arrhythmia and ischemic heart disease; 29 with acute and chronic lung disease; 7 with liver disease; 13 with gall stone and post-cholecystectomy; 7 with renal stone and acute pyelonephritis; 9 with malignancy; 1 with acute appendicitis. Among liver disease, we selected the acute hepatitis and liver cyst with a normal function. Among malignancy, we selected the post-operation of colon cancer free from bone metastasis. Several patients had two or more concomitant diseases.

We excluded the following secondary osteoporosis due to the renal failure, endocrine disease, post-oophorectomy and hysterectomy. In addition, we excluded the following atherosclerotic disease: hyper-lipidemia, diabetes mellitus, hypertension and chronic collagen disease. Furthermore, aortic aneurysm or dissection and the marked distortion of aorta were excluded. We excluded the long-term bedridden patients caused by the cerebrovascular disease or osteoarthrosis, the patients under the therapy of calcium supplement, vitamin-D and hormonal drug, and then the malnutritional patients with post-gastrectomy or mental anorexia.

Measurement of abdominal aortic calcification: Using single-energy CT equipment (Hitachi Medico, CT-W400-20), we scanned the abdominal aorta and produced the images under the following conditions: X-ray voltage 120 KV; current amplitude 250 mA; slice thickness 1 cm; slice interval 0 cm; scanning field 30 cm; scanning time 4.5 sec; window level ±50; window width 250; calculation matrix size 320×320 pixels [15)].

As shown as Figure 1, we scanned the relevant abdomen of each patient in a supine position, and set the region of interest (ROI) on the abdominal aorta by the rectangular square (Fig. 1, Upper left). For clarifying the outline of aortic calcification, we magnified an image of abdominal aorta on the display by zooming five folds (Fig. 1, Upper right), and established a CT threshold number of 115 Hounsfield Unit (HU). This CT number was determined to produce an adequate calcification image along the internal or external margin of aortic wall by visual inspection. In order to discriminate more clearly the outline of aortic calcification, we developed the binary image over this CT threshold number in a black color (Fig. 1, Lower left). By means of handmanual-tracing the outline of individual calcification sites using a track ball, we calculated their areas of aortic calcification (Fig. 1, Lower right). As shown in Figure 2, we summed up the calcification volume (CV; cm^3) by adding the individual area of calcified sites within 10 slices upward over the bifurcation of abdominal aorta. On the other hand, we summed up the aortic volume (AV; cm^3) by adding each ellipsoidal circle using the maximum and minimum diameters of external margin of aortic wall within 10 slices. Subsequently, we calculate the aortic calcification index (ACI;%) of CV to AV[16)].

BMC measurement in lumbar vertebral body: As shown in Figure 3, we measured the BMC of vertebral bodies with the lumbar CT using a calibration phantom (Chugai Pharmaceutical, B-MAS) according to the method of Cann et al.[14)] and Fujii et al.[15)] We examined under the same CT scanning conditions as the abdominal aorta[16)]. During CT examination, the phantom was attached closely to the lumbar back of the patient in a supine position, with CT equipment at an angle for scanning a slice as perpendicular as possible to the midplane of the vertebral body. Thus, both the vertebral body and the phantom system were scanned simultanecusly (Fig. 3, Upper left). Subsequently, we set the ROI in the

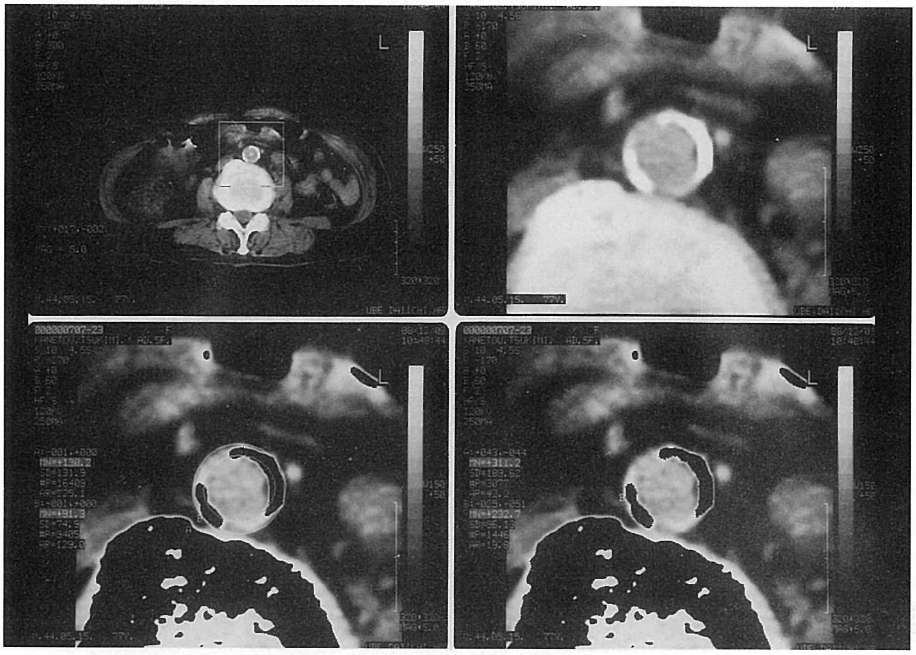

Fig 1. The measurement method of abdominal aortic calcification by computed tomography (CT). Upper left: The image of abdominal aorta is set at the region of interest (ROI) by rectangular square on the display for zooming. Upper right: Abdominal aorta is magnified by zooming five folds. Calcification sites in aortic wall appear as a white image. Lower left: Aortic calcification over the CT threshold number represent as a binary black image. Lower right: The calcification area is hand-manually traced around the outline of calcified sites in aortic wall.

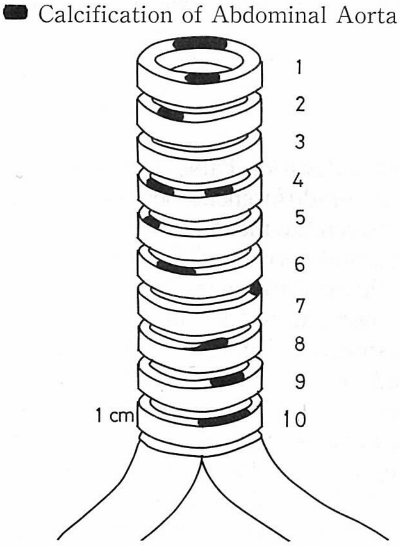

Fig 2. The measurement method for aortic calcification index (ACI; %) of calcification volume (CV; cm^3) to aortic volume (AV; cm^3) within 10 slices upward over the bifurcation of abdominal aorta.

spongious bone of the vertebral body using the largest ellipsoidal circle excluding a cortical bone and a nutritional foramen on the display. Then, we calculated the mean CT number in the ROI of vertebral body (Fig. 3, Lower right). Similarly, we set the five ROIs on five standard substances in the calibrated phantom by using round circles, and calculated the mean CT numbers within the five ROIs (Fig. 3, Upper right and lower left). Five standard substances were composed of the following concentrations of $CaCO_3$: 32.31, 80.17, 133.47, 177.03, and 223.66 mg/cm^3, in this order[15]. The first regression line was calculated by the least squares method using both the mean CT number and the corresponding $CaCO_3$ concentration of each standard. By applying the mean CT number of the vertebral body to the first regression line, BMC (mg/cm^3) was obtained. In all patients, we simultaneously scanned the 2nd, 3rd and 4th lumbar vertebral bodies (Fig. 3, Upper left). Results from the 3rd body were used as a

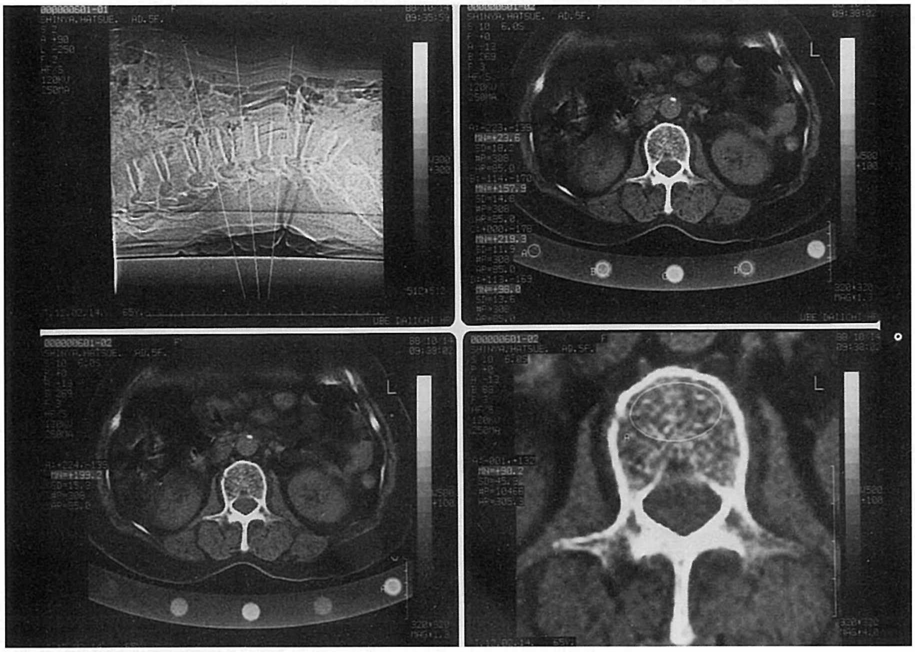

Fig 3. The measurement method for bone mineral content (BMC) of the lumbar vertebral body.
Upper left: Scanogram and Scanning line of lumbar vertebral body in a scout-view image.
Upper right and lower left: The simultaneous scanning image of both the vertebral body and the calibrated phantom. Five regions of interest (ROIs) are set on five standard substances of phantom.
Lower right: ROI is set on the spongious bone of vertebral body by the largest ellipsoidal circle, excluding a cortical bone and a nutritional foramen.

representative BMC for most patients. In patient with compression fractures or marked calluses formation complicated of trabecular microfracture in the 3rd vertebral body, results from the 2nd or 4th body were used as a representative BMC. Patients with severe compression fractures or marked scoliosis throughout the three vertebral bodies were excluded[16].

Thus, we studied the age- and sex-differences between the ACIs and between the BMCs, and investigated the relationships between ACIs and BMCs in every decades of age in both sexes.

Statistics analysis: The statistics was used by the paired and non-paired Student's t-test. Correlation analysis was calculated by the first regression line using a least square. P value lower than 0.05 was significant. The mean value represent as mean ± standard deviation (SD).

Results

Abdominal aorta: Table 1 summarises the age- and sex-differences between the mean ages, between the mean diameters of abdominal aorta and between the AVs. There were no significant differences between the mean ages of men and women in every decades of age. As shown in Figure 2, the mean diameter averaged by the maximum and minimum diameter of external margin of the aortic wall was calculated in the upper scan on the 1st slice, in the middle on the 5th, and in the lower on the 10th, respectively. In men, almost of the upper, middle or lower mean diameters and mean AV increased in proportion to aging. On the other hand, in women, all of the upper, middle and lower mean diameters increased with aging, but AV increased in order of the 60s, 80s, 70s and 90s decades of age. Compared between men and women, many of both the mean diameters and AVs in men were significantly larger than those in women (60s:Upper diameter p< 0.01, Lower diameter and AV p<0.05; 70s: Upper and lower diameters p<0.01; 80s: Upper, middle or lower diameters and AV p<0.01).

ACI: Table 1 and Figure 4 showed the age- and sex-differeneces between the CVs and

Table 1. The mean ages of patients, and the mean diameters, aortic volumes (AVs), calcification volumes (CVs), and aortic calcification indexes (ACIs) of abdominal aorta.

Decade of age		Mean age (yrs)	Mean diameter of arotic wall Upper (cm)	Middle (cm)	Lower (cm)	AV (cm³)	CV (cm³)	ACI (%)
Men	(n= 81)							
60s	(n= 16)	65.6±2.7	2.6±0.3	2.1±0.4	1.9±0.3	32.6± 9.5	3.4±4.1	9.1± 9.5
70s	(n= 28)	75.1±2.5	2.7±0.3	2.1±0.2	2.1±0.3	35.6± 8.8	2.6±2.4	7.4± 6.6
80s	(n= 32)	82.8±2.8	2.7±0.3	2.1±0.2	2.0±0.3	37.8± 6.5	3.7±3.9	10.0±10.3
90s	(n= 5)	92.4±2.5	2.9±0.4	2.3±0.2	2.0±0.2	41.3±10.3	3.5±3.4	8.7± 8.0
Women	(n=142)							
60s	(n= 18)	65.0±2.4	2.3±0.3**	1.8±0.2	1.7±0.2*	26.5± 3.5*	0.4±0.6**	1.2± 1.8**
70s	(n= 61)	75.2±2.8	2.4±0.3**	1.9±0.5	1.8±0.2**	31.2±12.1	2.0±2.4	6.1± 7.1
80s	(n= 55)	83.4±2.5	2.5±0.3**	1.9±0.3**	1.8±0.2**	30.4± 6.4**	3.3±2.9	10.9± 9.3
90s	(n= 8)	91.5±1.6	2.6±0.9	2.3±0.9	2.0±0.5	33.3± 7.5	3.5±2.4	11.8± 9.2

Abbreviations: n=the number of patients; ACI=Aortic calcification index (%) of calcification volume (CV) to aortic volume (AV); * =p<0.05, * * =p<0.01 of different significances between men and women; Mean values represent as mean±SD.

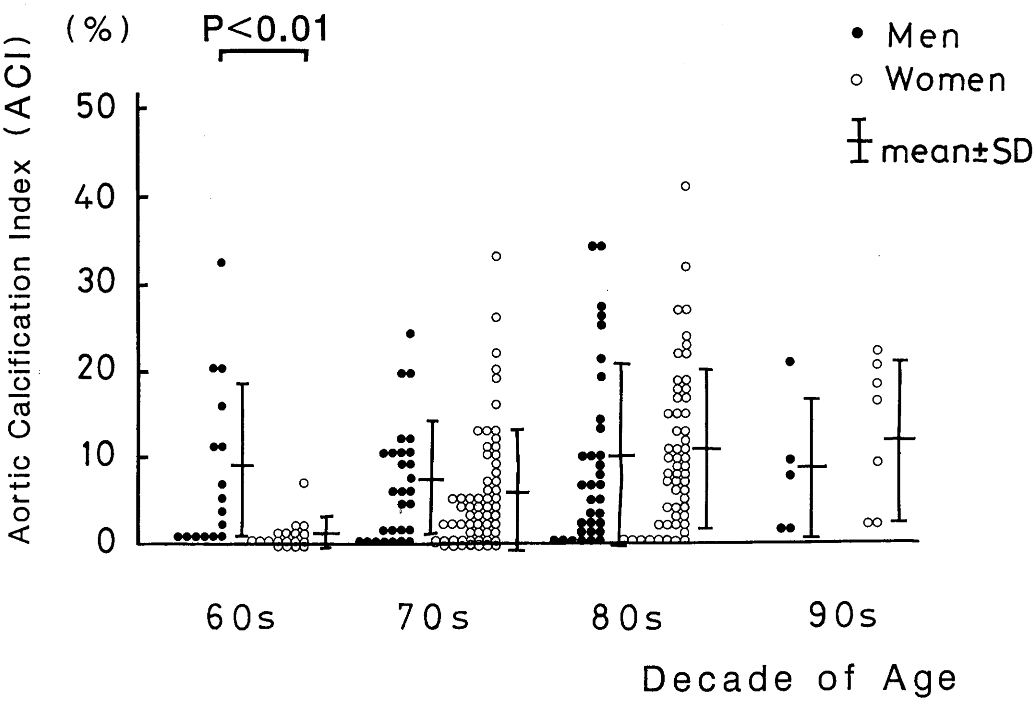

Fig 4. The age- and sex-differences between the aortic calcification indexes (ACIs). Closed circles are men. Open circles are women.

between the ACIs. In men, CV increased gradually in order of the 70s, 60s, 90s and 80s decades of age, but ACI increased in order of the 70s, 90s, 60s and 80s. On the other hand, in women, both CV and ACI increased with aging. Compared the CVs and ACIs between men and women, CVs in men were significantly larger in the 60s (Men 3.4±4.1 vs Women 0.4±0.6 cm^3; $p<0.01$), or larger in the 70s (NS), but less in th 80s and 90s (NS) than those in women. Whereas, ACIs in men were significantly higher in the 60s (Men 9.1±9.5

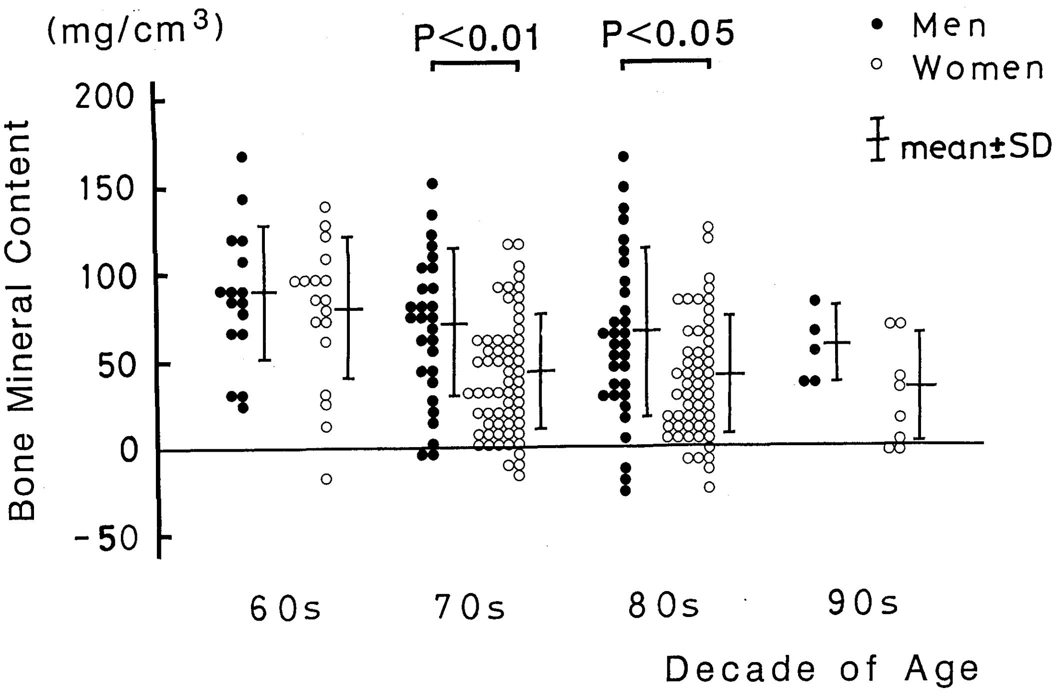

Fig 5. The age- and sex-differences between the bone mineral contents (BMCs). Closed circles are men. Open circles are women.

Table 2. The mean ages of patients, bone mineral contents (BMCs) of the lumbar vertebral body, the numbers of patients who were used by the 2nd, 3rd or 4th vertebral bodies as a representative BMC, the first regression rates by phantom, and correlation rates between BMCs and ACIs.

Decade of age		Mean age (yrs)	Vertebral body for BMC 2nd(n)	3rd(n)	4th(n)	Regression rate by phantom	BMC (mg/cm³)	Correlation rate BMC vs ACI	
Men	(n= 81)								
60s	(n= 16)	65.6±2.7	—	15	1	0.973±0.009	89.7±39.8	−0.366	NS
70s	(n= 28)	75.1±2.5	1	25	2	0.970±0.010	71.2±42.0	−0.117	NS
80s	(n= 32)	82.8±2.8	1	28	—	0.967±0.023	65.2±47.7	+0.012	NS
90s	(n= 5)	92.4±2.5	2	2	1	0.975±0.015	56.9±22.2	−0.760	NS
Women	(n=142)								
60s	(n= 18)	65.0±2.4	—	17	1	0.971±0.012	80.1±41.7	−0.229	NS
70s	(n= 61)	75.2±2.8	7	47	7	0.974±0.009	43.5±33.5**	−0.371	p<0.01
80s	(n= 55)	83.4±2.5	4	44	7	0.978±0.011	40.8±33.7*	−0.334	p<0.01
90s	(n= 8)	91.5±1.6	2	5	1	0.978±0.016	31.5±31.3	−0.118	NS
Total	(n=223)	77.8±7.6	20	183	20	0.973±0.014			

Abbreviations: n=the number of patients; * =p<0.05, * * =p<0.01 of different significances between men and women; NS=Not significant; Values represent as mean±SD.

vs Women 1.2±1.8%; $p<0.01$), or higher in the 70s (Men 7.4±6.6 vs Women 6.1 ±7.1 %, NS) than those in women. Contrastly, ACIs in women were higher than those in men, but not significant in the 80s and 90s (80s:Men 10.0±10.3 vs Women 10.9±9.3%,NS; 90s:Men 8.7±8.0 vs Women 11.8±9.2%, NS).

BMC: Table 2 and Figure 5 showed the age- and sex-differences between the BMCs. As a representative BMC, 20 patients were used by the 2nd lumbar vertebral body, 183 were the 3rd, 20 were the 4th, respectively. In men, 15 patients were used by the 3rd body and 1 was by the 4th in the 60s, respectively. One was used by the 2nd body, 25 by the 3rd, and 2 by the 4th in the 70s. Four were used by the 2nd and 28 by the 3rd in the 80s. Moreover, two were used by the 2nd, 2 by the 3rd, and 1 by the 4th in the 90s, respectively. Correspondingly in women, 17 patients were used by the 3rd body, and 1 was used by the 4th in the 60s. Seven were used by the 2nd, 47

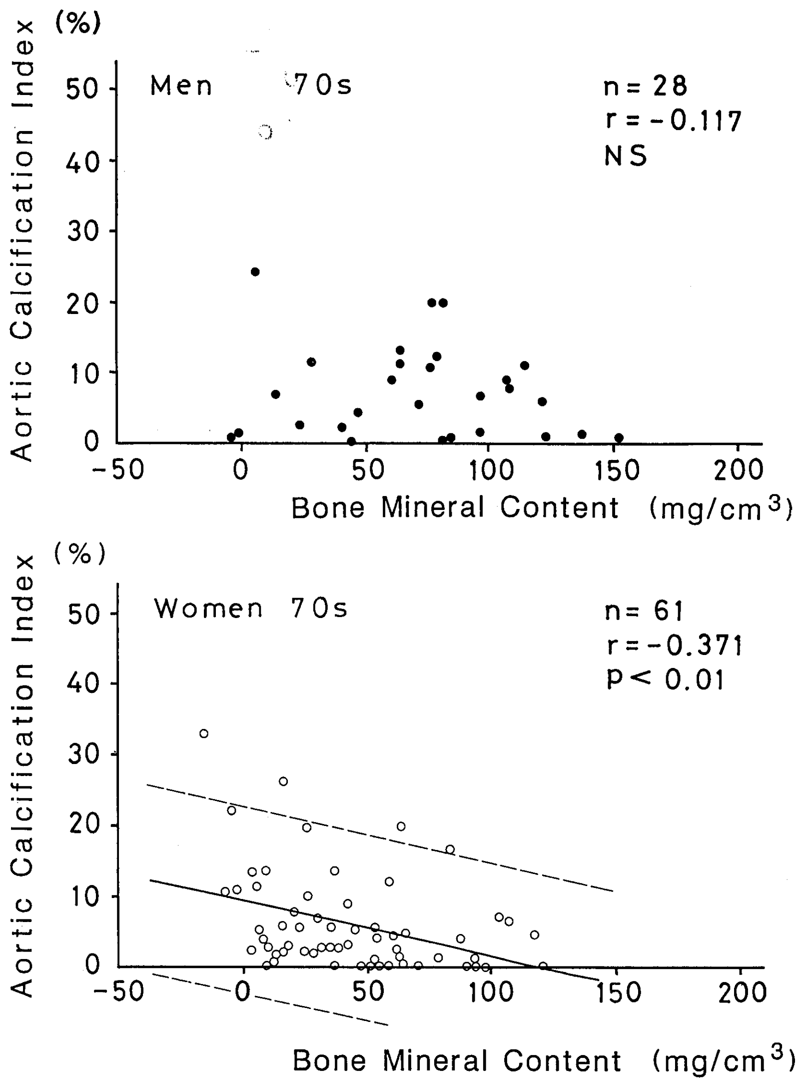

Fig 6. The correlative relations between ACIs and BMCs in the 70s decade of age. Upper figure: men. Lower figure: women.

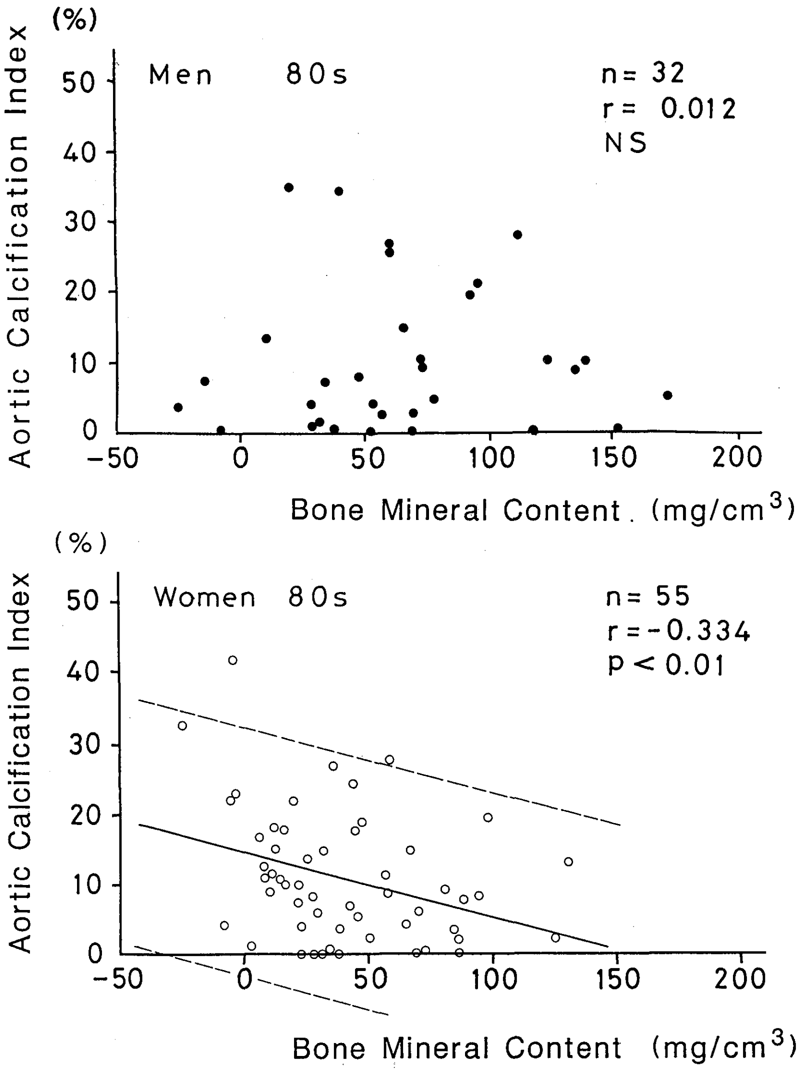

Fig 7. The correlative relations between ACIs and BMCs in the 80s decade of age. Upper figure: men. Lower figure: women.

by the 3rd, and 7 by the 4th in the 70s. Four were by the 2nd, 44 by the 3rd, and 7 by the 4th in the 80s. Similarly, 2 were by the 2nd, 5 by the 3rd, and 1 by the 4th in the 90s, respectively. For a representative BMC, an incidence of usage by the 2nd or 4th vertebral body was higher in women than in men (NS). The mean rate of the first regression line by phantom system to calculcate the BMC for all patients was 0.973±0.014.

In both men and women, BMCs decreased in proportion to aging. Compared between men and women, all of BMC in women were lower than all in men. Especially in the 70s and 80s, BMCs in women were significantly less than those in men (70s:Men 71.2±42.0 vs Women 43.5±33.5 mg/cm^3, $p<0.01$; 80s:Men 65.2±47.7 vs Women 40.8±33.7 mg/cm^3, $p<0.05$).

Relationship between ACI and BMC: As shown in Figure 6 and 7, there were significant negative correlations between ACIs and BMCs in women in the 70s and 80s (70s:$r=-0.371$, $p<0.01$; 80s:$r=-0.334$, $p<0.01$), but no relations between both of them in men (Table 2). In the 60s and 90s, there were no correlations between both of them in men and women (Table 2).

Discussion

Abdominal aortic calcification and osteoporosis: The elderly men and women have a decreased physical activity, and have a low intestinal-absorption and an excess urinary-excretion of calcium due to mental, nutritional and metabolic disorders[17]. Similarly, serum levels of growth hormone, insulin-like growth factor, vitamin-D, calcitonin and sex-hormone decrease, but a serum level of parathyroid hormone increases with aging[17)18]. Especially in the elderly women, decreased female-sex hormone depresses the testosterone secretion, vitamin-D metabolism, and osteoblast cell activity[19], and affects the parathyroid gland and osteoclast cell activity with a high level of serum phosphate to cause the postmenopausal osteoporosis[20)22]. On the other hand, postmenopausal women had the elevated serum cholesterol and triglyceride[23)24]. Decreased female-sex hormone depresses the adrenal gland activity and lipoprotein receptor of liver cell, and elevates the serum lipids. Especially, the surgical-menopaused women after hysterectomy or bilateral oophorectomy had a marked increased incidence of atherosclerotic lesions and a severely high risk of ischemic heart disease[25]. Thus, a low serum level of female-sex hormone causes the osteoporosis and atherosclerosis, since aortic smooth muscle cells in aortic wall and osteoblast in bone have a estrogen receptor[26)27]. In the elderly Japanese women, osteoporosis occurs more frequently than in European and American women[28]. Therefore, the postmenopausal disorders in elderly women worsen more severely in Japan than in the other countries.

The present study revealed that there were significant negative correlations between abdominal aortic calcification and bone mineral content of lumbar vertebrae in women at the 70s and 80s decades of age. The common medical conditions inducing the osteoporosis are hypogonadism (in men), early hysterectomy or oophorectomy (in women), subtotal gastrectomy, hyperthyroidism, long-term bedridden due to hemiplegia, glucocorticoid and anticonvulsion drug[17]. In this study, the patients under these medical conditions and the patients with postmenopausal hypercholesterolemia were excluded. Experimental report in rats demonstrated that the calcium decalcified from bone shifts to other soft tissues of the aortic wall, kidney, heart, muscle and spleen in this order, by calcium-mobilization phenomenon[29]. The calcium deposition sites on aortic wall are mainly atheromatous plaque and elastic fiber[30)31]. In these sites, the calcium-binding proteins are contributed to calcium deposition in the form of the extracellular matrix combined with calcium and phosphate, similar to the matrix in bone tissue[32)–34]. Perhapse, results of the present study suggested that the calcium decalcified from bone due to postmenopausal osteoporosis may shift to the abdominal aortic wall by calcium-mobilization phenomenon, and/or may form the aortic calcification by the excess depositions of calcium-binding proteins.

Abdominal aortic calcification: Abdominal aortic calcification occurs more frequently in the lower region than in the upper region[3]. The lower region shows a relative fewer artifact than the upper region during CT scanning. Therefore, we examined the aortic calcification in the lower region. CT examination revealed the various forms of aortic calcification: a round solidation within aortic wall; a thin streak along the wall; a swollen mass bulging out the external margin of aortic wall; a thickened ring narrowing the inner cavity of aorta. In many cases, aortic calcification showed a vague indistint contrast even when the image was magnified on the display. CT number of abdominal aorta had many influences of the volume effect phenomenon, and the overshooting or undershooting due to gastro-intestinal air, renal or cholepancreatic stone, and thoracic or vertebral bone[4]. Therefore, in order to calculate the aortic calcification without these influences by the condition of the simplicity, facility, and objectivity in some extent, we established an optimal CT threshold number (115 HU) to discriminate the calcification from aortic wall. In the case of undershooting, this CT number delineated the calcification as a relative smaller area than the visually-described area. Conversely in the case of overshooting, this CT number enabled us to discriminate the outline of calcification free from artifacts. The semi-quantitative point counting methods by circumferential ratio of calcification sites to aortic wall are proposed as the maximum point of 8 or 16 by visual inspection[12)13)]. Compared these methods, our method was considered as an effective usage of reflecting the changes in various forms of aortic calcification.

Bone mineral content: The quantitative CT (QCT) method using a calibration phantom provides a highly accurate measurement of BMC in spongious bone of vertebral body. QCT makes it possible to study the BMC free from artificial noisy factors, such as changes in temperature or humidity, the model of CT equipment, and the body type of the patient[14)15)]. In the vertebral body of osteoporotic patients, BMC by the spongious bone provides a higher sensitivity than that by the cortex or spicular bone[35)]. In addition, the decalcification rate from the vertebral body is the same as that from whole body bones[36)]. Nevertheless, with the single-energy QCT we used, a beam hardening phenomenon at both the cortical bone of vertebral body and the fatty tissue of spongious bone affects the CT number to result in an underestimated negative number in some patients[37)]. Dual-energy QCT is used to resolve this phenomenon, but exposes the patients to much X-ray irradiation. In practice, there is little difference between the results by single- and dual-energy QCT in values of the mean and standard deviation[37)]. Moreover, the elderly patients have frequently many fractures and deformities in cortex bone of vertebral body, and a high incidence of trabecular microfracture with calluses formation in spongious bone[38)]. Therefore, a representative BMC could not be obtained with only one result of the 3rd vertebral lumbar body. Even a recent high-resolution method of dual-energy X-ray absorptometry has some unavoidable limitations related to fractures and deformities[39)]. So far as BMC of lumbar vertebrae is examined in the elderly, it is impossible to avoid the unstable factors related to bone deformities or fractures even by any method.

Clinical significance of abdominal aortic calcification: There were some reports concerning the abdominal aortic calcification. These reports demonstrated that there are a high incidence of brain atrophy and a high risk of coronary artery disease in patients with marked calcification of abdominal aorta[2)5)12)]. In the near future of super-aging society in Japan, aortic calcification as well as osteoporosis will be a significant clinical problem as a prophylaxic medicine of senile diseases.

References

1) Eikeles, A.: A comparative radiological study of calcified atheroma in males and females over 50 years of age. *Lancet,* **2**: 714-715,1957.
2) Eggen, D.A., Strong, J.P. and MoGill, H.C.: Calcification in the abdominal aorta; Relationship to race, sex, and coronary atherosclerosis. *Arch. Pathol.,* **78**:575-583,1964.
3) Mitchell, J.R.A. and Adams, J.H.: Aortic size and aortic calcification: A necropsy study. *Atherosclerosis,* **27**:437-446,1977.
4) Dixon, A.K., Laurence, J.P. and Mitchell, R. A.: Age-related changes in the abdominal aorta shown by computed tomography. *Clin Radiol.,* **35**:33-37,1984.
5) Witteman, J.C.M., Kok, F.J., van Saase, J.L. C.M. and Valkenburg, H.A.: Aortic calcification as a predictor of cadiovascular mortality. *Lancet,* **2**: 1120-1122,1986.
6) Anderson, J.B., Barnett, E. and Nordin, B.E. C.: The relation between osteoporosis and aortic calcification. *Br. J. Radiol.,* **37**: 910-912,1964.
7) Dent, C.E., Engelbrecht, H.E. and Godfrey, R. C.: Osteoporosis of lumber vertebrae and calcification of abdominal aorta in women living in Durban. *Br. Med. J.,* **4**:76-79,1968.
8) Fujita, T., Okamoto, Y., Sakagami, Y., Ota, K. and Ohata, M.: Bone changes and aortic calcification in aging inhabitants of mountain versus seacoast communities in the Kii Peninsula. *J. Am. Geriatr. Soc.,* **32**:124-128, 1984.
9) Limpert, J.D., Vogelzang, R.L. and Yao, J.S. T.: Computed tomography of aortoiliac atherosclerosis. *J. Vasc. Surg.,* **5**:814-819,1987.
10) Hyman, J.B. and Epstein, F.H.: A study of

the correlation between roentgenographic and post-mortem calcification of the aorta. *Am. Heart J.,* :540-543,1954.

11) Herfkens, R.J., Higgins, C.B., Hricak, H., Lipton, M.J., Crooks, L.E., Sheldon, P.E., and Kaufman, L.: Nuclear magnetic resonance imaging of atherosclerosis disease. *Radiology,* **148**:161-166,1983.

12) Takeda, S., Watanabe, H., and Matsuzawa, T.: Association of atherosclerosis with increased atrophy of brain matter in the elderly. *J Am. Geriatr. Soc.,* **34**:259-262,1986.

13) Tsushima, M.:The clinical classification of atherosclerosis and non-invasive methods for diagnosis of atherosclerosis(in Japanese). *Jpn. J. Atherosclerosis Soc.,* **13**:783-791,1985.

14) Cann, C.E., Genant, H.K., Kolb, F.O. and Ettinger, B.: Quantitative computed tomography for prediction of vertebral fracture risk. *Bone,* **6**:1-7,1985.

15) Fujii, Y., Tsunenari, T., Tsutsumi, M., Miyauchi, A., Yamada, M., Fukase, M., Yoshimoto, Y., Okuno, Y., Kusakabe, H., Miyoshi, K., Fukunaga, M., Morita, R. and Fujita, T.: Quantitative computed tomography: Comparison of two calibration phantoms. *J. Bone Mineral Metabolism,* **6**:71-74,1988.

16) Sugihara, N., Matsuzaki, M. and Kato, Y.: Ectopic calcification of the abdominal aorta and bone mineral content of vertebrae(in Japanese). *Jpn. J. Geriatr.,* **26**:256-264,1989.

17) Riggs, B.L.R. and Melton-III, L.J.: Involutional osteoporosis. *N. Engl. J. Med.,* **314**: 1676-1686,1986.

18) Epstein, S., Bryce, G., Hinman, J.W., Miller, O.N., Riggs, B.L., Hui, S.L. and Johnston, C. C.: The influence of age on bone mineral regulating hormones. *Bone,* **7**:421-425,1986.

19) Aloia, J.F., Cohn, S.H., Waswani, A., Yeh, Y. K., Yuen, K. and Ellis, K.: Risk factors of postmenopausal osteoporosis. *Am. J. Med.,* **78**:95-100,1984.

20) Orimo, M. and Shiraki, M.: Role of calcium regulating hormones in the pathogenesis of senile osteoporosis. *Endocrinol. Japon,* **1**:1-6, 1979.

21) Gallagher, J.C., Riggs, B.L., Jerpbak, C.M. and Arnaud, C.D.: The effect of age on serum immunoreactive parathyroid hormone in normal and osteoporotic women. *J. Lab. Clin. Med.,* **95**:373-385,1980.

22) Duarte, B., Hargis, G.R. and Kukreja, S.C.: Effects of estradiol and progesterone on parathyroid hormone secretion from human parathyroid tissue. *J. Clin. Endocrinol. Metab.,* **66**:584-587,1988.

23) Shibata, H., Matsuzaki, T. and Hatano, S.: Relationship of relevant factors of atherosclerosis to menopause in Japanese women. *Am. J. Epidermiol.,* **109**:420-424,1979.

24) Hjortland, H.C., McNamara, P.M. and Kannel, W.B.: Some atherogenic concomitants of menopause; The Fragmingham study. *Am. J. Epidermiol.,* **103**:304-311,1976.

25) Witteman, J.C.M., Grobbee, D.E., Kok, F.J., Hofman, A. and Valkenburg, H.A.: Increased risk of atherosclerosis in women after the menopause. *Br. Med. J.,* **298**:642-644,1989.

26) Nakao, J., Orimo, H., Ooyama, T. and Shiraki, M.: Low serum estradiol levels in subjects with arterial calcification. *Atherosclerosis,* **34**:469-474,1979.

27) Eriksen, E.F., Colvard, D.S., Berg, N.J., Graham, M.L., Mann, K.G., Spelsberg, T.C. and Riggs, B.L.: Evidence of estrogen receptors in normal human osteoblast-like cells. *Science,* **241**:84-86,1988.

28) Nordin, B.E.C.: International patterns of osteoporosis. *Clin. Orthop.,* **45**:17-30,1966.

29) Orimo, H., Terashita, K., Nakamura, T. and Ohshita, J.: Ca and atherosclerosis. *J. Nutr. Sci. Vitaminol., 31(Suppl.)* S33-S36,1985.

30) Ross, R.: The pathogenesis of atherosclerosis; An update. *N. Engl. J. Med.,* **314**:488-500,1986.

31) Sandberg, L.B., Soskel, N.T. and Leslie, J.G.: Elastin structure, biosynthesis, and relation to disease states. *N. Engl. J. Med.,* **304**:566-579,1981.

32) Levy, R.J., Lian, J.B. and Gallop, P.: Atherocalcin, A γ-carboxyglutamic acid containing protein from atherosclerotic plaque. *Biochem. Biophys. Res. Commun.,* **91**:41-49, 1979.

33) Keely, F.W. and Sitartz, E.E.: Characterization of proteins from the calcified matrix of athero-sclerotic human aorta. *Atherosclerosis,* **46**:29-40,1983.

34) Dmitrovsky, E. and Boskey, A.L.: Calcium-acidic phospholipid-phosphate complexes in human atherosclerotic aorta. *Calcif. Tissue Int.,* **37**:121-125,1985.

35) Jones, C.D., Laval-Jeantet, A.M., Laval-Jeantet, H.M. and Genant, H.K.: Importance of measurement of spongious vertebral bone mineral density in the assessment of osteoporosis. *Bone,* **8**:201-206,1987.

36) Gallagher, J.C., Goldgar, D. and Moy, A.: Total bone calcium in normal women; Effect of age and menopause status. *J. Bone. Min.*

Res., **2**:491- 496,1987.

37) Pacifici, R., Susman, N., Carr, P.L., Birge, S. J. and Avioli, L.V.: Single and dual energy tomographic analysis of spinal trabecular bone: A comparative study in normal and osteoporotic women. *J. Clin. Endocrinol. Metab.,* **64**:209-214,1987.

38) Hansson, R. and Roos, B.: Microcalluses of the trabeculae in lumbar vertebrae and their relation to the bone mineral content. *Spine,* **6**:375-380,1981.

39) Pacifici, R., Rupich, R., Griffin, M., Chines, A., Sueman, N. and Avioli, L.: Dual energy radiography versus quantitative computed tomography for the diagnosis of osteoporosis. *J. Clin. Endocrinol. Metab.,* **70**:705-710, 1990.