Table 2
Age-adjusted hazard ratios for death by baseline parameter, Cox's hazard model

Item	Hazard ratio	95% CI		P
BMI (+1 kg/m^2)	0.95	0.89	1.01	0.10
25-OHVD (< 50 nmol/l/≥50 nmol/l)	1.54	1.22	1.97	<0.01
GFR (+1 stage)	1.20	0.93	1.57	0.16
Smoking (yes/no)	7.51	1.22	24.67	0.03
Alcohol drinking (yes/no)	2.92	1.02	6.54	0.04
Diabetes mellitus (yes/no)	1.31	0.88	2.20	0.21
Hypertension (yes/no)	1.24	10.1	1.52	0.04
Hyperlipidemia (yes/no)	1.13	0.90	1.44	0.29
Dementia (yes/no)	1.79	1.09	2.87	0.02
Malignancy (yes/no)	4.76	2.92	7.50	<0.01
Cardiovascular event (yes/no)	2.13	1.40	3.21	<0.01
Prevalent fracture (yes/no)	1.79	1.20	2.66	<0.01
Therapy pattern (BP+ES+V/no)	1.27	0.86	1.86	0.23
Therapy pattern (BP+ES/V+no)	0.68	0.36	1.20	0.19
BMD category (osteopenia/normal)	0.62	0.26	1.36	0.23
BMD category (osteoporosis/osteopenia)	3.09	1.62	6.65	<0.01

CI; Confidence interval, BMI; body mass index, 25-OHVD; 25-hydroxyvitamin D, GFR;. Glomerular filtration rate, BP; bisphosphonate, ES; estrogen, V; vitamin, BMD; bone mineral density.

than 0.2 and the missing values for 25-OHVD were imputed by using multiple imputation method [34]. Finally, Kaplan–Meier plots were shown by prognostic factors, with log-rank test. All the *P*-values presented are taken from the two-side test and were considered to be significant when they were less than 0.05. All the analyses were performed using the SAS software, Version 9.1 (SAS Institute Inc. Carly, NC, USA).

Results

In the 1232 women enrolled in this study, the mean and SD range of observational period was 6.9±3.6 years with the longest observation time being 14.0 years. Table 1 lists the baseline characteristics of the subjects. The mean and SD range for age of the participants at baseline was 63.9±10.5 years old (mean±SD). Vitamin D insufficiency and deficiency as evaluated by the baseline 25-OHVD level was found in 331 (44.3%) and 20 (2.7%) of the participants, respectively. Twenty subjects showed 25-OHVD levels suggestive of vitamin D deficiency with none showing obvious clinical signs and symptoms of osteomalacia. In contrast to the data reported for the Caucasian population, the subjects with smoking or alcohol habit were markedly fewer. A total of 531 (43.1%) subjects were diagnosed as having osteoporosis at baseline and the prevalence of osteoporosis in these subjects correlated with the advancing years as well as the presence of prevalent fracture. Prevalent vertebral or long bone fractures were observed in 294 (23.9%) subjects. A total of 107 subjects (8.7%) were dead during the observation that lasted until the end of April 2007. The median period of observation to their death was 5.3 years. The death rate was 12.6 deaths/1000 person-year. Survival was confirmed in a total of 790 (64.1%) who were censored on their last clinic visit. The remaining 335 participants (27.2%) were lost to follow-up through regular clinical visits during the observation period. Of the 335 participants lost to follow-up, 122 (9.9%) subjects were found to be bedridden or to have been admitted to nursing homes, with the remaining 213 (17.3%) lost to follow-up for

Table 3
Multivariate Cox's regression analyses of prognostic factors for death

Item	Hazard ratio	95% CI		P
Age (+5 year)	1.73	1.51	1.98	<0.01
25-OHVD (<50 nmol/l/≥50 nmol/l)	2.17	1.27	3.72	0.01
Smoking (yes/no)	4.29	0.81	22.80	0.09
Drinking (yes/no)	2.16	0.73	6.38	0.16
Cardiovascular event (yes/no)	1.48	0.93	2.36	0.09
Dementia (yes/no)	1.54	0.89	2.66	0.12
Malignancy (yes/no)	5.60	3.36	9.31	<0.01
BMD category (osteopenia/normal)	0.72	0.32	1.65	0.44
BMD category (osteoporosis/normal)	2.14	1.22	3.75	0.01

CI; Confidence interval, 25-OHVD; 25-hydroxyvitamin D, BMD; bone mineral density. Backward variable selection method with criterion $P<0.2$ is used to reduce model.

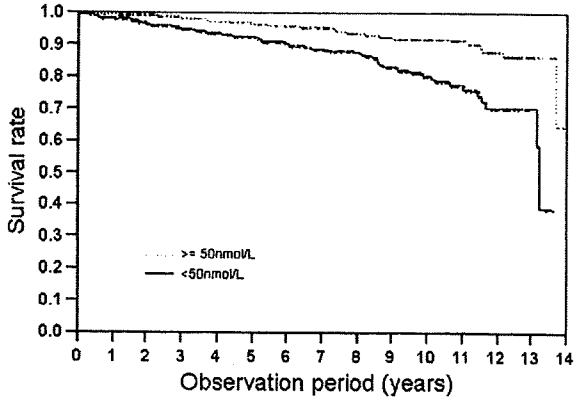

Fig. 1. Kaplan–Meier plots of survival by serum 25-hydroxyvitamin D level. 25-OHVD <50 nmol/l denotes deficiency and insufficiency; and ≥50 nmol/l, normal and borderline. There is a significant difference between the 25-OHVD categories (log-rank test; $P<0.01$).

unknown reasons. There was no difference in the rate of subjects lost to follow-up between those with osteoporosis and without ($P=0.56$). The causes of the subjects' death were vascular event (30 cases, 28.0%), cancer (23 cases, 21.5%), senile decay (23 cases, 21.5%), other (11 cases, 10.3%) and unknown (20 cases, 18.7%). Of the 30 subjects who died due to vascular events, 22 subjects (73.3%) had previous histories of cardio- or cerebrovascular events at baseline, and of the 23 who died of cancer, 16 (69.6%) had a history of malignancy, indicating that the remaining 8 and 7 deaths, respectively, due to vascular events and cancer, were incidental events during the observation. The subjects in the osteoporosis group showed a lower baseline prevalence of diabetes mellitus (3.2 versus 6.6%; $P<0.01$) and dyslipidemia (29.6 versus 43.3%; $P<0.01$) than those in the non-osteoporosis group. The baseline prevalence of hypertension (42.3 versus 40.4%) and cardio- or cerebrovascular events (12.9 versus 10.4%) in the osteoporosis group or non-osteoporosis group was not statistically significantly different ($P>0.05$). The baseline prevalence of and dementia was significantly higher in the osteoporosis group than those in the non-osteoporosis group (7.2 versus 2.9%; $P<0.01$). Meanwhile, there were no significant differences between osteoporosis and non-osteoporosis groups in baseline prevalence of malignancies (7.8 versus 7.6%; $P>0.05$). There was no difference in serum 25-OHVD levels between the subjects with a history of co-morbidities or those without and in the osteoporosis group or non-osteoporosis group ($P>0.05$). Cox's regression analysis was performed to evaluate the relationship between death and each of the baseline parameters with adjustment for age. 25-OHVD, presences of cardio-

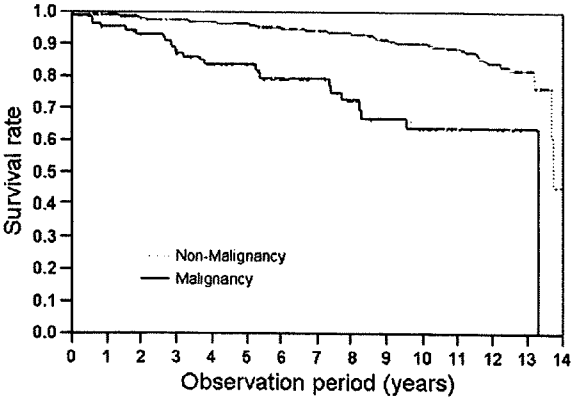

Fig. 2. Kaplan–Meier plots of survival by the presence or absence of malignancy. The prevalence of malignancy in baseline is associated with a significantly lower survival rate (log-rank test; $P<0.01$).

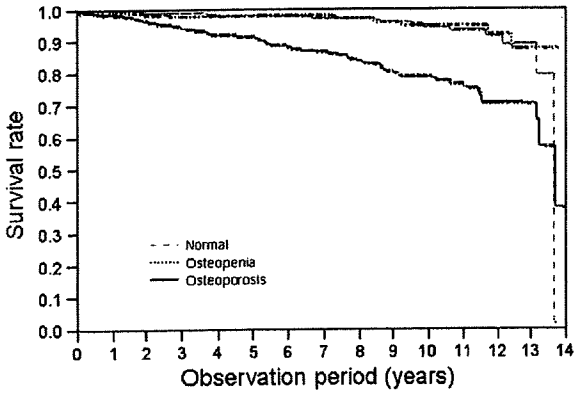

Fig. 3. Kaplan–Meier plots of survival by BMD category. Osteoporosis is diagnosed in accordance with the criteria of the Japanese Society for Bone and Mineral Research. Those with osteoporosis are associated with a significantly lower survival rate (log-rank test; $P<0.01$).

and cerebrovascular events, dementia, malignancy, smoking, drinking and prevalent fractures, and BMD, all indicated a significant correlation with death ($P<0.05$; Table 2). Multiple regression analysis was performed to evaluate the relationship between mortality and selected baseline parameters by the backward selection method (Table 3). Age, 25-OHVD, presence of malignancy and BMD at baseline were associated with mortality. The subjects who were treated with 1-alpha-OHVD3 for their osteoporosis during the observation period, were subtracted from the study in order to determine whether the hazard ratio of 25-OHVD for mortality was changed or not. However, the hazard ratio of 25-OHVD for mortality did not change when it was compared with before the subtraction of the subjects and after. Kaplan–Meier plots indicate a significant deference in survival rate when stratified by 25-OHVD (Fig. 1), presence of malignancy (Fig. 2) or stratified by BMD (Fig. 3). Serum 25-OHVD level <50 nmol/l, presence of malignancy or the presence of osteoporosis was shown to be associated with a significantly higher mortality rate (log-lank test; $P<0.01$).

Discussion

It has been well documented that the fractures are associated with increased mortality, especially 1 year after hip fractures [11,12]. However, little information has been available regarding the significance of baseline BMD on subsequent death in Asian population. The primary aim of the present study was to clarify whether Japanese postmenopausal women with osteoporosis are associated with a higher mortality rate than those without. The Cox hazard model demonstrated in the present study that osteoporosis is associated with a higher mortality rate than those without after adjustment for confounding factors. Therefore, we can conclude that osteoporosis not only in Caucasians but also in Asians may be associated with higher mortality than those without osteoporosis. However, the number of deaths was not sufficient to account for the difference in the cause of death between those with osteoporosis and the control subjects. The prevalence of low BMD is an important component of the risk for fracture. There are many reports that indicate the relationship between incident fractures and mortality in osteoporosis [5–14]. Therefore, fracture is thought to be a good predictor of mortality in subjects with low BMD. However, we should predict the mortality before fracture event. To clarify an early predictor of mortality, we investigated whether or not low BMD represented a risk factor for mortality in an ambulatory sample of Japanese patients. The study results demonstrate that low BMD is a significant independent risk factor for future death. However, in the present study, our model did not include prevalent fractures to predict subsequent death. This may indicate that low BMD is a better predictor for death than prevalent fractures. The exact reason why prevalent fractures did not predict future death, is unknown. But the clinical significance of fracture effect on death is more important in incident fracture than prevalent fracture, because the present participants may consist of the survivors from fresh fracture, which may affect the survival. The participants with osteoporosis showed a lower baseline prevalence of diabetes and dyslipidemia as risk factors for death. Furthermore, the baseline prevalence of hypertension, vascular events and malignancy between the osteoporosis and non-osteoporosis groups was not significantly different. The higher prevalence of dementia found at baseline in the osteoporosis group compared to that in the non-osteoporosis group may have contributed to the higher mortality rate in the present study. Although pre-existing dementia was not a significant risk factor for future death, it might represent possible causes of low activity in daily life and result in low BMD. Therefore, it is necessary to investigate whether or not dementia accounts for low bone density or whether it may be associated with subsequent low bone density. The prevalence of malignancy was another independent significant risk for future death in the present study. This phenomenon is thought to be within our expectation because some of the prevalent malignancies may have relapses. The low level of 25-OHVD observed frequently in elderly people [35–37] was found to be another significant independent risk factor for future death. A recent report indicates that lower serum 25-OHVD levels are associated with a higher risk of nursing home admission or mortality rate [24], suggesting that a lower (<50 nmol/l) 25-OHVD level may be used as an indicator of frailty. The higher risk for death in people with low 25-OHVD levels may be explained by the risk of sarcopenia [38], falls and low physical performance [39]. Furthermore, low 25-OHVD levels are reported to be associated with autoimmune disease, cancer, cardiovascular disease or diabetes [37,40,41]. A meta-analysis consisted of 18 randomized controlled trials reported that the intake of ordinary doses of vitamin D supplements seems to be associated with mortality [42]. However, this report stated that the relationship between mortality and baseline level of vitamin D would be required the further clarification [42]. Thus, the result of the present study may have some contribution to the issue between vitamin D and survival in elderly people. However, the present study showed no significant association between low 25-OHVD and these morbid states.

Our study has some limitations. First, there was a possible sampling bias that could have led to the participants having more serious illness than the general population, because our study population consisted of those who sought medical consultation for various reasons. However, the prevalence of co-morbidities, which had a potentially causal relationship to mortality, seemed to be unrelated to the higher mortality in the osteoporosis group. Second, 213 subjects who were lost to follow-up were included for analysis in this study; therefore, the survival rate reported may not be completely accurate. However, we think that those lost to follow-up were possibly distributed equally between the survivors and dead, because the subjects with no co-morbidity may have been less motivated to visit the clinic and those with serious illness may have dropped out due to their loss of mobility. Third, the participants with osteoporosis used some type of drug for osteoporosis therapy; therefore, the association between the incident fractures and mortality was unclear. A recent study using zoledronic acid for secondary prevention of fractures indicated that the zoledronic acid-treated group after hip fracture was associated with lower mortality than the control subjects [43]. Therefore, the mortality rate in osteoporosis may have been underestimated in the present study because of the treatment given for osteoporosis. However, despite the treatment given, the mortality rate in the osteoporosis group was higher than in the control subjects, clearly indicating that those with osteoporosis had a higher mortality rate than those without. Finally, we only studied Japanese women living in a rural area so that to confirm our finding, further investigation in a large sample of people from entire Japan or metropolitan areas is required.

Although the present investigation had several limitations, this is the first to address the association between low BMD or serum 25-

OHVD levels and mortality in Japanese women. In summary, the study findings suggest that the presence of osteoporosis and lower levels of 25-OHVD represent potentially powerful risk factors for mortality.

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Possible risk factor for postmenopausal women: Postprandial hypertriglyceridemia

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Abstract

Aim: To explore the clinical implications of postprandial hypertriglyceridemia in postmenopausal Japanese women.

Methods: Postprandial blood samples were collected from 91 women at their initial visit, with fasting blood samples collected within the following month to examine their lipid profiles. These women were grouped into normotriglyceridemia (fasting/postprandial triglycerides [TG] < 150; $n = 36$), mild postprandial hypertriglyceridemia (fasting TG < 150, postprandial TG ≥ 150, <225; $n = 27$), moderate postprandial hypertriglyceridemia (fasting TG < 150, postprandial TG ≥ 225; $n = 19$) and hypertriglyceridemia (fasting TG ≥ 150; $n = 9$) by using 225 mg/dL as the cut-off value for postprandial hypertriglyceridemia.

Results: The subjects were 54.1 ± 7.8 years old; their duration of menopause, 6.0 ± 7.7 years; body mass index, 21.4 ± 4.0 kg/m^2; postprandial TG concentration, 189 ± 110 mg/dL; and fasting TG concentration, 109 ± 50 mg/dL. Approximately 50% ($n = 46$) of the women had normal fasting TG (fasting TG < 150), but high postprandial TG (postprandial TG ≥ 150). Approximately 10% ($n = 9$) of the women had hypertriglyceridemia (fasting TG ≥ 150 mg/dL). In those with postprandial hypertriglyceridemia ($n = 46$), postprandial TG negatively correlated with high-density lipoprotein cholesterol (HDL-C), while fasting TG showed no such correlation with HDL-C.

Conclusion: Postprandial TG may provide a better understanding of lipid metabolism in postmenopausal women.

Key words: coronary heart disease, hormone replacement therapy, hypertriglyceridemia, postmenopause, postprandial hypertriglyceridemia.

Introduction

A decrease in the circulating estrogen concentration after menopause causes abnormalities in lipid metabolism leading to an increase in the incidence of ischemic heart disease in postmenopausal women. The results of the Women's Health Initiative, a large-scale randomized control trial,[1] demonstrated in 2002 that female patients receiving hormone replacement therapy (HRT) were associated with a hazard ratio of 1.24 for coronary artery disease, indicating that estrogen does not confer cardiac protection.

Although estrogen decreases low-density lipoprotein cholesterol (LDL-C) and increases high-density lipoprotein cholesterol (HDL-C),[2–5] it also carries the risk of ischemic heart disease and stroke partly because of an associated increase in triglycerides (TG).[6] Hypertriglyceridemia may decrease the size of LDL particles and contribute to an increase in insulin resistance.[7] All of these factors may therefore lead to the development of arteriosclerotic lesions.

Postprandial hypertriglyceridemia is also considered an independent predictor of ischemic heart disease.[8] We therefore compared fasting and postprandial

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blood samples to investigate the clinical implications of postprandial hypertriglyceridemia in postmenopausal Japanese women.

Methods

The subjects comprised 91 women who participated in an outpatient health maintenance program for middle-aged and elderly women implemented at our department between November 2000 and March 2003. Postprandial blood samples (taken after lunch) were collected from the subjects after lunch at their initial visit, with their fasting blood samples taken after 12 h of fasting during the following month. Normotriglyceridemia was defined as fasting TG < 150 mg/dL and the subjects were subgrouped into the following four groups by using 225 mg/dL as the cut-off value for postprandial hypertriglyceridemia: normotriglyceridemia ($n = 36$), mild postprandial hypertriglyceridemia ($n = 27$), moderate postprandial hypertriglyceridemia ($n = 19$) and hypertriglyceridemia ($n = 9$).

Statistical analyses were performed using Microexcel 2002. The Mann–Whitney *U*-test was used to compare the fasting lipid profiles of the four groups as stratified by TG concentration. A paired *t*-test was used to compare postprandial normotriglyceridemia and postprandial hypertriglyceridemia for lipid metabolism. ANOVA was used to test for differences in HDL-C between postprandial and fasting TG concentration. For all analyses performed, a *P*-value of 0.01 was considered statistically significant.

Results

Baseline characteristics of subjects

The mean age of the 91 women was 54.1 ± 7.8 years. Their physical findings were as follows: height, 156.5 ± 5.1 cm; body weight, 53.8 ± 7 kg; and body mass index, 21.4 ± 4 kg/m^2. Their duration of menopause was 6 ± 7.7 years.

Breakdown of results by TG concentration

The mean postprandial TG concentration was 187 ± 111 mg/dL, and the mean fasting TG concentration was 108 ± 50 mg/dL, with the mean difference (postprandial–fasting) being 85 ± 81 mg/dL. The postprandial TG concentration, compared with the fasting TG concentration, increased in 78 women (86%), did not change in one woman (1%) and decreased in 12 women (13%).

Table 1 Baseline characteristics of the women including their fasting and postprandial triglyceride (TG) concentrations ($n = 91$)

	n	%	Mean ± SD
Age (years)			54.1 ± 7.8
BMI (kg/m^2)			21.4 ± 4.0
<25	83	91.2	
≥25	8	8.8	
TC (mg/dL)			226.9 ± 34.0
LDL-C (mg/dL)			140.1 ± 32.5
HDL-C (mg/dL)			62.0 ± 15.7
Fasting TG (mg/dL)			108.9 ± 50.4
<150	82	90.9	
≥150	9	9.1	
Postprandial TG (mg/dL) (Fasting TG < 150)			187.0 ± 111.4
<150	36	40.0	
≥150, <225	27	30.0	
≥225	19	20.9	

BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Relationship between postprandial TG and fasting TG concentrations (Table 1)

The TG concentration was normal (<150 mg/dL) in the fasting state but high in the postprandial state in 46 women, who accounted for approximately 50% of the women. True hypertriglyceridemia with a fasting TG concentration of ≥150 mg/dL was seen in nine women, comprising approximately 10% of all women. The postprandial TG concentrations in all of these women with hypertriglyceridemia were high (≥150 mg/dL).

Fasting serum lipid profile by TG classification

We found that HDL-C and TC were lower in those with postprandial hypertriglyceridemia than in those with normal TG ($P < 0.01$) (Table 2). Among the 46 women with postprandial hypertriglceridemia, we found a significant negative correlation between postprandial TG and HDL-C ($r = -0.43$, $P = 0.0081$) (Fig. 2). Fasting TG had a negative but insignificant correlation with HDL-C in these women.

Discussion

Hyperlipidemia is considered a risk factor for arteriosclerotic diseases. Examination of lipid profiles in aged women shows that TC rapidly increases to a higher level in these women than in men once they are over the age of 50, which is the average age at onset of menopause. In women, HDL-C remains uniform up to

Table 2 Fasting lipid profiles of four groups by triglyceride (TG) classification (mean ± SD)

Group	Age (years)	BMI (kg/m^2)	TG (mg/dL)	HDL-C (mg/dL)		LDL-C (mg/dL)	TC (mg/dL)		Arteriosclerosis index (TC-HDL)/HDL
Normotriglyceridemia† ($n = 36$)	52.3 ± 7.0	21.6 ± 2.4	87 ± 26	70 ± 15		150 ± 26	237 ± 26		2.5 ± 0.7
Mild postprandial hypertriglyceridemia ($n = 27$)	55.4 ± 7.0	21.6 ± 2.6	100 ± 29	64 ± 14	*	148 ± 32	230 ± 32	*	2.9 ± 1.0
Moderate postprandial hypertriglyceridemia ($n = 19$)	54.8 ± 7.2	22.0 ± 2.0	106 ± 26	52 ± 10		134 ± 36	212 ± 45		3.5 ± 0.8
Hypertriglyceridemia ($n = 9$)	58.4 ± 12.3	23.3 ± 2.9	229 ± 52	45 ± 9		118 ± 28	209 ± 24		3.8 ± 0.8

*$P < 0.01$.
†We defined normal triglyceridemia as fasting TG < 150 mg/dL using 225 mg/dL as the cut-off value for postprandial hypertriglyceridemia.
BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TC-HDL, total cholesterol high-density lipoprotein.

the age of approximately 50, and then decreases slightly from then on, while TG concentration increases from the age of approximately 30 and peaks at the age of approximately 60. Therefore, in postmenopausal women, lipid metabolism declines with age and is characterized by an increase in TC, a decrease in HDL, and an increase in TG associated with a rapid decrease in the estrogen concentration.

When the circulating estrogen concentration falls after menopause, the number of LDL receptors in the liver decreases and LDL remains in the blood.[9] It is believed that the associated increase in TG concentration decreases the size of LDL particles, which promotes the progression of arteriosclerosis.[10] In this regard, it is reported that hormone replacement therapy (HRT) not only improves lipid metabolism but also exerts many anti-arteriosclerotic effects, such as antioxidant and vasodilatory effects. Binding estrogen (conjugated equine estrogen) not only produces desirable effects on lipid metabolism, it is also thought to induce hypertriglyceridemia.[3] Therefore, when starting HRT, lipid metabolism status needs to be assessed and patients with abnormalities need to be individually evaluated.

TC and LDL-C are recognized as risk factors for ischemic heart disease.[7] However, based on the Framingham Study,[11] HDL-C and TG are identified as more important risk factors for ischemic heart disease in postmenopausal women. In recent years, the concept of the metabolic syndrome as a high-risk pathology that causes arteriosclerotic diseases has also been put forward, and diagnostic criteria for this syndrome have been established.[12] The diagnostic criteria for the metabolic syndrome are the accumulation of visceral fat and the presence of at least two of the following factors: abnormal lipid metabolism, hypertension and abnormal glucose metabolism. Abnormal lipid metabolism is defined as TG concentrations ≥150 mg/dL or HDL-C concentrations <40 mg/dL.[12] Hypertriglyceridemia and a low blood HDL-C concentration are therefore specified in the diagnostic criteria together.[13,14] Patients with type 2 diabetes mellitus who have postprandial hypertriglyceridemia are reported to have a significant thickening of the vascular walls.[15] This abnormal condition suggests that there is also a correlation between abnormal lipid metabolism, including hypertriglyceridemia, and abnormal glucose metabolism (insulin resistance), which are included in the diagnostic criteria for the metabolic syndrome.

Postprandial TG concentration is markedly affected by food intake and needs to be viewed as a factor

that varies considerably with diet.[14,16] Even in adults without ischemic heart disease risks, it is believed that an association exists between chronic hypertriglyceridemia and increases in plasma concentrations of biochemical markers of inflammation and endothelial activation.[7] Postprandial TG concentration is higher in women with ischemic heart disease,[17] indicating that postprandial hypertriglyceridemia is an important risk factor for arteriosclerosis and ischemic heart disease. A study showed that postprandial (non-fasting) TG concentration is an independent predictor of ischemic heart disease and is of greater clinical significance than the fasting TG concentration.[8] A subanalysis of the same study also showed that the association between TG and ischemic heart disease was not substantially affected by TC or HDL-C concentrations, suggesting that postprandial TG has an independent role in ischemic heart disease risk.[8] This is because the TG concentration is said to peak at 6–8 h postprandially, and persists for much of the day.[18,19]

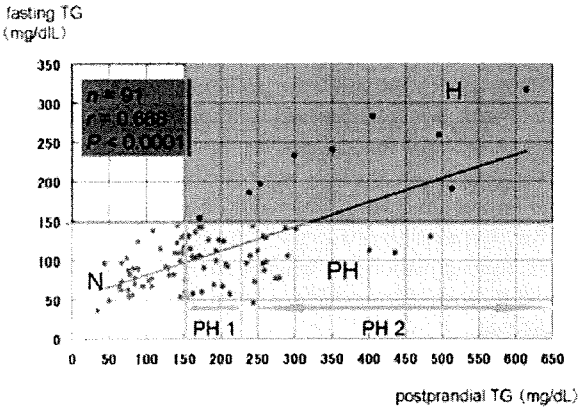

Figure 1 Relationship between postprandial triglycerides (TG) and fasting TG concentrations. H, hypertriglyceridemia (fasting TG ≥ 150 mg/dL); N, normotriglyceridemia (fasting TG < 150, postprandial TG < 150 mg/dL); PH 1, mild postprandial hypertriglyceridemia (fasting TG < 150, postprandial TG ≥ 150, <225 mg/dL); PH 2, moderate postprandial hypertriglyceridemia (fasting TG < 150, postprandial TG ≥ 225 mg/dL).

Postprandial (nonfasting) TG concentration is approximately 50% higher than the fasting TG concentration. Therefore, we consider 225 mg/dL an appropriate cut-off value for postprandial hypertriglyceridemia in those with a normal fasting TG concentration below 150 mg/dL. In our study, 46 of the 91 subjects, or approximately 50% of all subjects, had a high postprandial TG concentration (≥150 mg/dL) despite having a normal fasting TG concentration (Fig. 1). Through comparison of the four groups by using a postprandial TG concentration of 225 mg/dL as the cut-off value, we showed a significant difference in TC and HDL-C concentrations between the moderate postprandial hypertriglyceridemia group and the normotriglyceridemia group only. Furthermore, HDL-C negatively correlated with the postprandial TG concentration. Thus, postprandial TG could provide a better understanding of lipid metabolism.

The prevalence of postprandial hypertriglyceridemia in postmenopausal women is high. When starting HRT, it is also important to determine how to avoid adverse cerebrovascular effects. By changing the route of administration of estrogen preparations from oral to transdermal and by reducing the estrogen dose, an increase in TG or inflammation markers can be inhibited. It has also

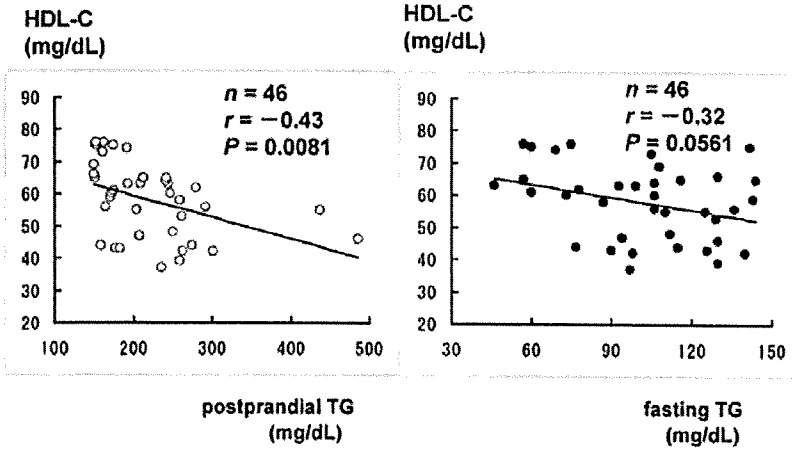

Figure 2 Correlation between high-density lipoprotein cholesterol (HDL-C) and postprandial or fasting triglyceride (TG) concentration in women with postprandial hypertriglyceridemia. Among the 46 women with postprandial hypertriglyceridemia, we found a significant negative correlation between their postprandial TG and their HDL-C ($r = -0.43$, $P = 0.0081$).

been found that progestin preparations not only reduce HDL-C but also inhibit vascular endothelial function, while natural progestin preparations have no such effects. Individual methods of administration therefore need to be investigated according to the characteristics of each HRT prescription.

In conclusion, we showed a high incidence of postprandial hypertriglyceridemia among postmenopausal women, and postprandial hypertriglyceridemia negatively correlated with HDL-C. Therefore, we conclude that postprandial TG could provide a better understanding of lipid metabolism. Measuring this parameter should be of value and may be used to screen postmenopausal women undergoing HRT so as to reduce cerebrovascular risks.

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ORIGINAL ARTICLE

Association between lumber bone mineral density and vascular stiffness as assessed by pulse wave velocity in postmenopausal women

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Abstract Recent studies have showed a significant correlation between vascular calcification and bone mineral density (BMD). Therefore, an investigation was carried out on the association between arterial stiffness, lumbar BMD and bone metabolic markers in Japanese postmenopausal women. Brachial-ankle PWV (baPWV) and BMD of the lumbar spine and serum bone-specific alkaline phosphatase (BAP) levels in 143 postmenopausal women were measured, where there was a significant negative correlation between baPWV and BMD ($r = -0.21$; $P = 0.0135$). An additional analysis included the remaining 75 subjects, but excluded subjects with hypertension and obesity. Here, a more negative correlation between baPWV and BMD ($r = -0.315$; $P = 0.006$), and a positive correlation between baPWV and BAP ($r = 0.248$; $P = 0.032$) were also significant. A group analysis, where the women were age matched and stratified into three groups of different bone density, i.e., normal BMD, osteopenic and osteoporotic, were further made. This showed lower PWV values in the normal BMD group than in the other two groups. A study also showed that the tertile with the highest BAP was associated with significantly higher PWV values than the other tertiles. However, when the multiple linear regression analysis was carried out, there was no correlation between PWV and BAP values. Low BMD and arterial stiffness show some correlation, suggesting that BAP may reflect the degree of arterial stiffness present.

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Keywords Bone mineral density · Brachial-ankle PWV · Bone-specific alkaline phosphatase · Arteriosclerosis · Osteoporosis

Introduction

Arteriosclerosis progresses with age, and the risk of arteriosclerosis in women increases significantly after menopause [1, 2]. On the other hand, bone mass decreases with age regardless of sex. However, women are at higher risk especially after menopause, when bone mass decreases rapidly due to a decrease in estrogen [3, 4]. It was recently shown that the degree of vascular calcification is significantly correlated with changes in bone density, suggesting that vascular sclerosis and decreased bone mass are closely linked pathological conditions [5–8].

Pulse wave velocity (PWV) can be used to measure the elasticity of arteries, thus providing an easy measure of progression of arteriosclerosis. Indeed, despite the fact that PWV values do not directly describe calcification of blood vessels, PWV is used as an effective measure of arteriosclerosis. Carotid-femoral PWV (cfPWV) has been a traditional method used to measure PWV. However, this method requires some technical skills. On the other hand, brachial-ankle PWV (baPWV), now available as a more convenient method, only requires placing blood pressure cuffs on the extremities. It has been reported that baPWV and cfPWV values are extremely well correlated within the same patient, suggesting that baPWV is as equally reliable as cfPWV as an index for the severity of arteriosclerosis as well as a prognostic indicator in the care of patients with hypertension [9, 10].

The most important objective of osteoporosis treatment lies in the prevention of bone fractures, which occur as

bone strength, a composite endpoint combining both bone quality and density, diminishes considerably. In clinical studies, an accurate evaluation of bone density and quality is carried out by using the dual-energy X-ray absorptiometry (DXA) method and by the use of appropriate bone metabolism makers.

A negative correlation between vascular sclerosis and BMD has already been reported [5–8]. However, DXA has seldom been used for evaluation of bone density, and studies exploring the association between vascular sclerosis and bone metabolism markers are very few.

This study aimed to elucidate the relationship between arteriosclerosis and osteoporosis in postmenopausal women by examining their baPWV, bone mineral density by using DXA, and bone metabolic markers for association among these variables.

Subjects and methods

Subjects

This study enrolled 143 postmenopausal women who visited the Menopause Clinic in our department from January 2004 to April 2005. Their menopausal status was confirmed by interview, where those who had not menstruated for 12 months were considered to be menopausal. Those who could not precisely recall the date of their last menstrual period or who did not answer the questionnaire were excluded from the study. None of the subjects had undergone hormonal replacement therapy or had taken any steroid hormones. Women who had hypertension, diabetes, dyslipidemia or osteoporosis took appropriate medication for the condition (Table 1).

Informed consent was obtained from every subject who enrolled in the study. The study protocol was then approved by the Ethics Committee of Tokyo Women's Medical University.

Measurement of pulse wave velocity

All subjects underwent brachial-ankle pulse wave velocity (baPWV) measurement as an index for arteriosclerosis, using a form pulse wave velocity/ankle brachial pressure index (form PWV/ABI) (Nippon Coli). Details of the methodology have been described previously [8].

The subjects were examined while resting in a supine position with the measurement device set to simultaneously record PWV, blood pressure, electrocardiogram and heart sounds. Electrocardiogram electrodes were placed on both wrists, and a heart sound microphone was placed over the left sternal border. The cuffs were wrapped around both arms and ankles and connected to the plethysmographic sensors to evaluate brachial and post-tibial arterial pressure waveforms and volume pulse forms in the subjects. The subjects were also connected to oscillometric sensors to measure blood pressure. baPWV was measured in all subjects after they had rested for at least 5 min. The mean left and the right baPWV values for each subject were used for analysis.

Table 1 Clinical characteristics of 143 women in this study

Age (years)	57.9 ± 8.3
Height (cm)	155.7 ± 5.2
Weight (kg)	55.3 ± 9.4
BMI (kg/m^2)	23.0 ± 3.6
sBP (mmHg)	128.3 ± 21.6
dBP (mmHg)	76.1 ± 12.2
iPTH (pg/ml)	48.3 ± 19.9
Ca (mg/dl)	9.2 ± 0.8
Urinary Ca/Cr	0.18 ± 0.39
P (mg/dl)	3.6 ± 0.4
NTx (nmolBCE/mmol Cr)	43.1 ± 20.0
BMD (g/m^2)	0.884 ± 0.154
PWV (cm/s)	1,450 ± 261
BAP (IU/l)	25.0 ± 11.2
No. of subjects with	
Hypertension	3
Diabetes mellitus	5
Dyslipidemia	44
Osteoporosis	25
Age at menopause (years)	48.0 ± 5.0

All results are presented as the mean ± SD

BMI body mass index, *sBP* systolic blood pressure, *dBP* diastolic blood pressure, *iPTH* intact parathyroid hormone, *NTx* urine cross-linked *N*-telopeptides of type 1 collagen, *BAP* bone alkaline phosphatase

Measurement of bone mineral density

Lumbar spine (L2–L4) BMD was measured by using DXA (QDR4500, Hologic Inc., USA) as an index for osteoporosis. BMD values were reported as grams per square centimeter.

Laboratory measurements

The following variables were evaluated: blood Ca, P and intact PTH levels; urine Ca/Cr ratios; bone alkaline phosphatase (BAP) levels; and urine cross-linked telopeptides of type I collagen (NTx).

Statistical analysis

Data were expressed as mean ± SD. Simple regression analysis was used to examine correlation between baPWV,

BMD and other clinical variables. Multiple regression analysis was further performed for baPWV, BMD and other clinical variables. A value of $P < 0.05$ was considered statistically significant.

Results

Table 1 summarizes the characteristics of the subjects. There was a significant negative correlation between PWV and BMD in the 143 patients studied ($r = -0.21$; $P = 0.0135$) (Table 2). When each of the parameters evaluated was examined for possible correlation with PWV and BMD, there was a positive correlation between PWV and blood pressure, with a stronger correlation found between PWV and systolic blood pressure ($r = 0.734$; $P < 0.0001$). A positive correlation was also present between PWV and bone ALP (BAP) ($r = 0.166$; $P = 0.047$) (Table 2). BMD showed a positive correlation with both body weight and BMI, where a stronger correlation was seen between BMD and body weight ($r = 0.506$; $P < 0.0001$) (Table 2). Given these results, patients with hypertension (defined as sBP 140 mmHg or higher or dBP 90 mmHg or higher), a factor affecting PWV values, and those with BMI less than 18.5 as well as those with BMI more than 25, a factor affecting BMD, were all excluded from the study. The remaining 75 subjects were subjected to further review. Analysis of these 75 subjects showed a more significant negative correlation between PWV and BMD

Table 2 Univariate analysis of clinical factors correlated with brachial-ankle pulse wave velocity (baPWV) and lumbar bone mineral density (BMD)

	With baPWV		With BMD	
	r	*P*	*r*	*P*
Age	0.587	<0.0001	0.283	0.0006
Height	0.311	0.0002	0.191	0.169
Weight	0.006	NS	0.506	<0.0001
BMI	0.128	NS	0.453	<0.0001
sBP	0.734	<0.0001	0.026	NS
dBP	0.564	<0.0001	0.074	NS
BMD/baPWV	0.206	0.0135	0.206	0.0135
Ca	0.072	NS	0.090	NS
P	0.148	0.0793	0.026	NS
Urinary Ca/Cr	0.044	NS	0.028	NS
iPTH	0.140	0.0947	0.017	NS
NTx	0.030	NS	0.051	NS
BAP	0.166	0.0470	0.018	NS

BMI body mass index, *sBP* systolic blood pressure, *dBP* diastolic blood pressure, *iPTH* intact parathyroid hormone, *NTx* urine cross-linked *N*-telopeptides of type 1 collagen, *BAP* bone alkaline phosphatase

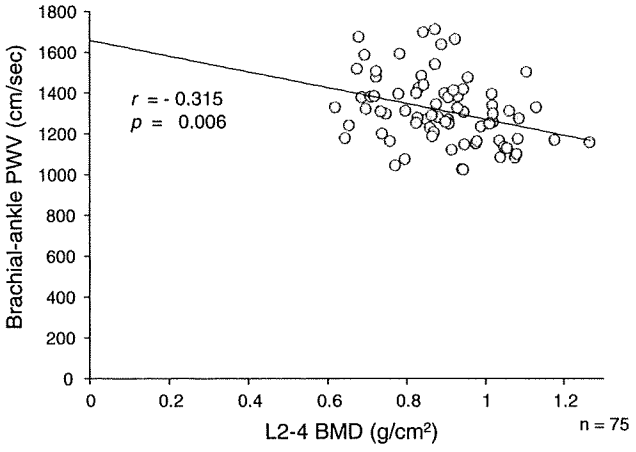

Fig. 1 An even stronger correlation was observed between L2–L4 BMD and PWV values after those with hypertension, a determining factor of PWV, and those with obesity as assessed by BMI, a determining factor of L2–L4 BMD, were excluded ($r = -0.315$; $P = 0.006$)

($r = -0.315$; $P = 0.006$) than in the earlier analysis from which no subjects were excluded (Fig. 1).

In order to eliminate the possibility of age affecting the results, the subjects were age-matched and then stratified into three groups by bone density, i.e., normal BMD ($n = 17$, L2–L4 BMD, 0.962 ± 0.085 g/cm^2), osteopenic ($n = 12$, 0.755 ± 0.029) and osteoporotic ($n = 9$, 0.673 ± 0.028). No significant difference was observed among these three groups concerning their age and blood pressure (Table 3). The subjects with normal BMD showed significantly lower PWV values than the other two groups (Fig. 2). Hence, a significant correlation between PWV and BMD was confirmed to be present even after adjustment for age among the subjects.

In the remaining 75 patients, PWV values showed a stronger positive correlation with the bone metabolism marker BAP ($r = 0.248$; $P = 0.032$) than when all subjects were included for analysis ($r = 0.166$; $P = 0.047$) (Fig. 3). Comparison of PWV values among the BAP tertiles showed that the tertile with the highest BAP showed significantly higher PWV values than the other tertiles ($P < 0.05$) (Fig. 4). A further examination by multiple regression analysis showed no correlation between PWV and BMD or between PWV and BAP (Table 4).

Discussion

Our study results demonstrate that PWV and BMD are negatively correlated in postmenopausal women. In addition, the greater the PWV values, and the more sclerotic the blood vessels are, the lower the lumbar L2–L4 BMD values. Of note, this negative correlation was shown to be particularly pronounced among women with normal

Table 3 Background factors in the three groups aged-matched and stratified by BMD

	Osteoporotic	Osteopenic	Normal BMD	*P*
Number	9	12	17	
BMD (g/m^2)	0.067 ± 0.028	0.755 ± 0.029	0.962 ± 0.085	<0.05
Age (years)	57.8 ± 8.1	57.6 ± 8.1	57.3 ± 5.2	NS
Height (cm)	155.0 ± 4.3	153.3 ± 4.4	157.2 ± 6.3	NS
Weight (kg)	49.6 ± 4.0	49.0 ± 5.1	54.9 ± 6.8	<0.05
BMI (kg/m^2)	20.6 ± 0.9	21.1 ± 1.8	22.1 ± 1.7	<0.05
sBP (mmHg)	120 ± 11	114 ± 13	11 ± 10	NS
dBP (mmHg)	71 ± 9	71 ± 8	66 ± 10	NS
iPTH (pg/ml)	47.2 ± 13.5	40.6 ± 11.9	46.8 ± 16.7	NS
Ca (mg/dl)	9.3 ± 0.3	9.3 ± 0.3	9.4 ± 0.6	NS
Urinary Ca/Cr	0.13 ± 0.08	0.16 ± 0.12	0.14 ± 0.07	NS
P (mg/dl)	3.5 ± 0.3	3.7 ± 0.2	3.6 ± 0.3	NS
NTx (nmolBCE/mmol Cr)	42.0 ± 22.5	48.2 ± 26.8	43.6 ± 21.1	NS
BAP (IU/l)	25.9 ± 8.1	24.6 ± 7.5	20.4 ± 6.5	NS

BMI body mass index, *sBP* systolic blood pressure, *dBP* diastolic blood pressure, *iPTH* intact parathyroid hormone, *NTx* urine cross-linked *N*-telopeptides of type 1 collagen, *BAP* bone alkaline phosphatase

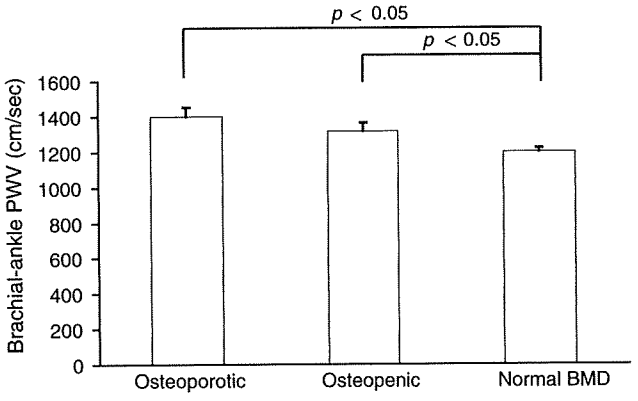

Fig. 2 The subjects in the normal BMD group showed significantly lower PWV values than the other two groups (1,201.1 ± 18.3 vs. 1,312.6 ± 49.0 cm/s, 1,201.1 ± 18.3 vs. 1,399.5 ± 54.1 cm/s; $P < 0.05$). All results are presented as mean ± SD. In these subjects, a significant negative correlation was shown between PWV and BMD even after they were adjusted for age

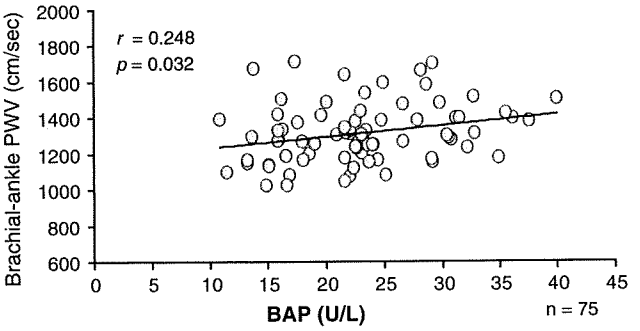

Fig. 3 PWV values showed a stronger positive correlation with BAP, a bone formation marker, in 75 subjects with normal blood pressure and BMI ($r = 0.248$; $P = 0.032$)

physique and blood pressure. Furthermore, this correlation was confirmed even when the data were adjusted for age, suggesting that decreased bone mass is a risk factor for atherosclerosis, independently of other risk factors, such as hypertension, diabetes or smoking. Our results are in agreement with the report of Hirose et al. [7] that demonstrated correlation between increased PWV and reduced calcaneal quantitative osteo-sono index as assessed by quantitative ultrasound (QUS). In recent years, similar findings have been reported not only in cross-sectional, but also in longitudinal studies [6, 11] that were conducted across races. These studies began to clarify the cellular mechanisms of pathogenesis implicated in both atherosclerosis and decreased bone mass [12, 13]. An osteoblast- or chondrocyte-like phenotypic transformation of vascular smooth muscle cells and myofibroblasts is assumed to be implicated in the process of vascular calcification, suggesting a role for osteochondral metabolism-associated factors in this process [14–16]. While aging and menopause are clinical risk factors for both atherosclerosis and osteoporosis, other factors, such as various inflammatory processes, oxidative stress and homocystein, are also reported as risk factors for both conditions [17].

The interrelationship between atherosclerosis and bone metabolism has been corroborated by the fact that anti-atherosclerotic and anti-resorptive agents exert effects on bone metabolism and on atherosclerosis [18, 19]. In this regard, statins as therapeutic agents for hypercholesterolemia are known to exert their anti-atherosclerotic effects through inhibition of HMG-CoA reductase, a key enzyme in the rate-limiting step of the mevalonate pathway; they have also been shown to mediate BMP-2 promoter activation. In both mouse calvarial cultures and in clinical trials [20, 21], statins were shown to increase the number of osteoblasts as well as new bone mass, suggesting a potential role for statins as a new class of pro-osteogenic

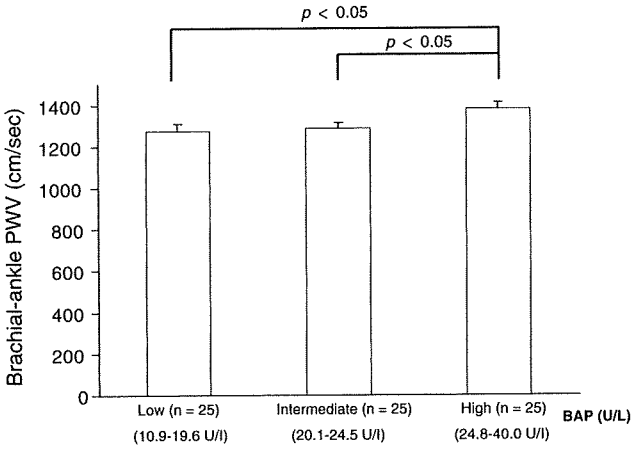

Fig. 4 The tertile with the highest BAP showed significantly higher PWV values than the other tertiles (1,308.8 ± 35.0 vs. 1,285.5 ± 27.6 cm/s, 1,308.8 ± 35.0 vs. 1,247.9 ± 35.6 cm/s; $P < 0.05$)

Table 4 Correlation of PWV and other factors as assessed by multiple regression analysis with a significance level of $P < 0.05$

Variable	Regression coefficient	*P* value	Standardized regression coefficient
Age	11.42	<0.001	262.58
Height	−3.72	0.115	−52.11
sBP	6.98	<0.001	408.06
BMD	−99.78	0.213	−35.27
BAP	1.89	0.171	42.06

sBP systolic blood pressure, *BAP* bone alkaline phosphatase

agents. On the other hand, bisphosphonates as anti-osteoporotic agents have been shown to suppress osteoclast activation as part of their mechanism of action that inhibits the mevalonate pathway [22]. Thus, together, these results suggest that statins and bisphosphonates may act on, and exert similar effects on, the same cells.

In our present study as well, BAP and PWV were found to be correlated, consistently with previous reports showing that when osteoporotic patients were stratified by presence or absence of aortic calcification, those with aortic calcification were associated with significantly higher BAP values [23]. It is also reported that BAP was significantly expressed in calcified vascular smooth muscle cells. Furthermore, in the presence of pro-inflammatory cytokines, there is an increase in the BAP level, thus further promoting vascular calcification [24]. These findings appear to point towards the possibility that BAP values reflect the degree of arteriosclerosis present and that osteoblast-like cells are implicated in arteriosclerosis.

In our analyses using multiple linear regression, we were unable to establish a clear relationship between PWV and BMD or between PWV and BAP. However, the results obtained from the stratified groups do not necessarily exclude the possibility of such relationship, as shown in a comparison of PWV values among the BAP tertiles. The main limitation of this study lies in the fact that the study subjects were not adequately uniform; the study subjects varied greatly in age and included those with medical conditions such as hypertension and diabetes. The limited availability of appropriate cases further enhanced the study limitation. Therefore, increasing the number of subjects, which also helps to ensure inclusion of uniform subjects, may contribute towards a better clarification of the relationship between bone and vasculature.

The management of bone metabolic disorders needs to focus not only on the disease per se, but also on the resulting vascular calcification that will likely lead to ectopic calcification, thus affecting the overall prognosis of affected patients. Mounting evidence suggests a strong correlation between vascular calcification and bone mineral content. While the implication of this finding remains to be further explored, current evidence appears to suggest a role for BMD measurement as an important index that assists in the management of vascular calcification.

It is suggested that patients with low bone mass should undergo careful monitoring for atherosclerosis to better manage the condition, where therapeutic intervention may also be considered. In a fast-aging society, such an approach is not only needed for the health of people and for the social care workers caring for them, but also for health economic reasons.

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備考欄

＊注：外枠線のまわりには、文字の記入、押印をしないでください。

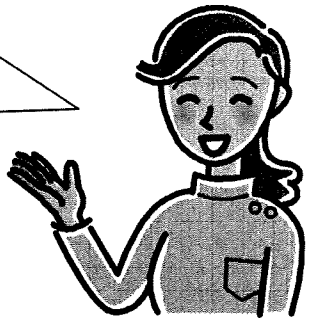
001

あなたの食習慣を詳しく知るための質問票

この質問票にていねいに答えることによって、
あなたの食習慣（栄養摂取状態）を詳しく知ることができます。

生活習慣病を予防し、健康な生活を送るためには、
自分の生活習慣を知ることは、とても大切です。

記入に必要な時間は、40分程度です。
（質問の内容が難しい場合には、あなたの家庭で食事の準備をおもにしているひとといっしょに考えながら、答えてください）



記入方法をよく読んで、記入もれのないように、気をつけてください。
太い黒の鉛筆で濃く記入してください。

記入方法

選択項目の枠内の　　を太い黒の鉛筆で濃くなぞって下さい。　枠線には触れないようにご記入ください。

良い例　　悪い例

毎日２回以上　　毎日２回以上　　毎日２回以上

数字は枠線に触れないように、丁寧にご記入ください。

0 1 2 3 4 5 6 7 8 9

フリガナ	
名前	
番号1（記入不要）	
番号2（記入不要）	
番号3（記入不要）	

あなたに適した食事量を計算するために必要です。最初にご記入ください

性別（○を記入）	生年月日（年号は○印を記入）
□ 男性　□ 女性	□ 大正　□ 昭和　□ 平成　□□ 年　□□ 月　□□ 日

今日（この質問票に答える日）の日付	現在の身長	現在の体重
平成 □□ 年　□□ 月　□□ 日	□□□ . □ cm	□□□ . □ kg

20歳ごろの体重（およそ）
□□□ . □ Kg

成人用.　1997.2.8版 2001.1.21改訂版　(01.10.13ﾚｲｱｳﾄ部分改訂)　Sasaki's DHQ43_3 OCR

002

あなたの最近 1か月間 の食事を考えてください

もっとも適当な答えを○で囲んでください

1 麺類(うどん・そば・ラーメンなど)のスープや汁を飲む量は、

ほとんど全部	8割	6割	4割	2割	ほとんど飲まない

2 家庭での味付けは外食と比べて、

薄口	少し薄口	同じくらい	少し濃い口	濃い口

3 お肉(牛肉や豚肉)の脂身は、

好んで食べていた	好きでも嫌いでもない	あまり食べなかった

4 鶏肉の皮は、

好んで食べていた	好きでも嫌いでもない	あまり食べなかった

5 次の食べ物を食べるとき、しょうゆ・ソース・たれ・つゆ・塩など、塩味のついた調味料をかけたり、つけて食べていたものをすべて○で囲んでください。
(ご注意)食べなかった食品には○をつける必要はありません。マヨネーズ・ケチャップ・ドレッシングは含みません。

カレーライス	さしみ	キャベツの千切り	てんぷら	白菜の漬け物	ほうれん草のおひたし

冷や奴	目玉焼き	甘塩鮭の焼き物	ぎょうざ	納豆	しらす干し	わかめの酢の物

6 上の質問で、あなたが使った、しょうゆ・ソース・たれ・つゆ・塩などの量は、

かなり多い	やや多い	ふつう	やや少ない	かなり少ない

7 食べる速さは、

かなり速い	やや速い	ふつう	やや遅い	かなり遅い

食事習慣を意識的に変えましたか

いいえ	1年前以内に変えた	1～2年前に変えた	数年前に変えた

8 医師、栄養士、その他専門家の指導で、食事のコントロールをしていましたか

いいえ	はい

次の食べ物をどのくらいの頻度で食べていましたか。 もっとも適当なものひとつを○で囲んでください。

1	カレーライス	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
2	シチュー	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
3	ミートソース	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
4	すし (一度に5個以上)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
5	手作り以外のぎょうざ、ハンバーグ、ミートボール、(外食、お持ち帰りを含む)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
6	外食をした回数は？ ただし、手作りの弁当は外食に含めません。 市販品を買って、家庭や職場で食べる場合や、職員食堂、学生食堂を利用する場合は、外食に含めます。	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった

さあ、スタート!!

003

最近1か月間の食事を考えてください
あなたがよく食べていたメニューと調理方法

①まれにしか食べなかったもの（1か月に1回未満）に「0（ゼロ）」をつけてください。

②次に、食べた頻度の高いものから順に、順番をつけてください。

同じくらいの頻度で食べるものには同じ順番をつけてください。

【記入例】

(1)魚介類を食べる時	
生 さしみ、すし、など	1
焼き物	1
煮物	0
揚げ物 てんぷらを含む	3
炒め物	2

もっともよく食べた

食べなかった

(1)魚介類を食べる時	
生 さしみ、すし、など	
焼き物	
煮物	
揚げ物 てんぷらを含む	
炒め物	

(2)肉類を食べる時	
生(たたきを含む)	
炒め物(外食)	
炒め物(家庭)	
揚げ物	
煮物(和風:すき焼き・肉じゃがなど)	
シチュー・カレー・ミートソース	
焼き肉・グリルなど	

(3)たまごを食べる時	
オムレツ	
目玉焼き	
玉子焼き	
ゆで卵	
生	

(4)野菜を食べる時	
漬け物	
生:サラダなど	
煮物の一部として	
炒め物の一部として 揚げ物・てんぷらを含む	
湯がいて	
蒸し物として	

最近1か月間に　飲んだお酒

飲んだ　｜　飲まなかった　｜　意図して止めていた　｜　　歳ごろ止めた

次のページに進んでください。

週か月のどちらかを○で囲んでから回数、及び1回に飲んだ量を記入してください。

種　類	頻　度	1回に飲んだ量
ビール・発泡酒など	週　月　に　回	大ビン663ml、缶330ml、ロング缶500mlを目安として　ml
日本酒	週　月　に　回	.　合
焼酎、泡盛	週　月　に　回	水で割る前。純焼酎、純泡盛として　.　合
酎ハイ	週　月　に　回	水で割った後の量。大グラス(300ml)で　.　杯
ウィスキー	週　月　に　回	水などで割る前。シングル(28ml)で　.　杯
ブランデー、コニャック、バーボン、ジンなどすべての蒸留酒を含みます。		
ワイン	週　月　に　回	ワイングラス(100ml)で　.　杯
その他	週　月　に　回	具体的ななまえ　　水で割る前の量で　ml

004

最近1か月間の食事を考えてください
あまり深く考えずに、第一印象でお答えください。

答え方

最近1ヶ月間に食べた頻度(回数)は？
ひとつを○で囲んでください。

例

毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった

頻度が「週1回」より多い場合は、
1回に食べていた量にお答えください。

頻度が「週1回」より少なかった場合は、
1回に食べていた量に答える必要はありません。

1回に食べていたおよその量は？
食品名の右側または下側()内の量(ふつう1回に食べる量)に比べて、
当てはまる項目をひとつ選び、○で囲んでください。

例

5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上

○印は、　　をなぞるようにご記入ください。
○印は、枠線からはみ出さないようにご記入ください。

良い例:　5割まで

悪い例:　5割まで　　5割まで

ここからお答えください

乳類など

1	牛乳 (150g、コップ1杯)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	週に1回以上の場合は、下の種類(ひとつ)と右の量に○ ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
		普通脂肪または高脂肪	低脂肪	スキムミルク	いずれともいえない・わからない				
2	ヨーグルト (1人前入り1個:100g)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	週に1回以上の場合は、下の種類(ひとつ)と右の量に○ ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
		砂糖入りかまたは砂糖を入れた	無糖	いずれともいえない	低脂肪	低糖			
3	チーズ	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(厚切り1枚、6Pチーズでは1個) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
4	カッテージチーズ	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(大さじ山盛り1杯:15g) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
5	乳飲料	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(ヤクルト、小1本:60g) (カルピス、うすめた状態でコップ1杯:200ml) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
6	バター	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(大さじ2分の1杯) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
7	マーガリン	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(大さじ2分の1杯) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			

005

肉類

1	挽き肉 (牛または豚)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(ハンバーグ・ハンバーガーとして1個 ミートソース1人前、ぎょうざ6個など:60g) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
2	鶏肉	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(主菜用1人前:80g、大きさとして卵2個弱) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
3	豚肉	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(主菜用1人前:80g、大きさとして卵2個弱) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
4	牛肉	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(主菜用1人前:80g、大きさとして卵2個弱) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
5	レバー (トリ、ブタ、ウシ)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(トリレバーの場合3個) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
6	ハム または ソーセージ	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(ハムではうす切り2枚(40g);ソーセージでは 小ウインナー3個、フランクフルト3分の1個(30g)) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
7	ベーコン (うす切り2枚:40g)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	サラミ(スライスで3枚) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			

魚介類(1)

1	さかなの干物	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(いわし・あじ・(中1匹)等、80g) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
2	骨ごと食べる魚	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(ししゃも1匹・しらす干し(小鉢に軽く1杯:20g))など ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
3	ツナ(油づけ)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	大さじ軽く3杯(サンドウィッチ中身1人分) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
4	うなぎ	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(蒲焼き1人前：2～3切れ) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
5	白身の魚	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(たい・かれい・たら等(1切れ、80g) および淡水魚) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
6	背の青い魚	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(さば(1切れ、80g)・いわし(中1匹、小2匹)・さんま(片身) ・あじ(大方身、小1匹)・ほっけ(小片身)・にしん(小片身)) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
7	赤身の魚	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(まぐろ・さけ・かつお・(1切れ、80g)等) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			

魚介類(2)

8	魚介練り製品 (2切れ、35g)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(かまぼこ、2切れ：ちくわ、半本) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
9	えび・かに	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(タイガーえび(えびフライ用)で3匹、80g) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
10	いか・たこ	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(寿司ネタとして、5個分、80g) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
11	かき(牡蛎)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(5個) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
12	他の貝類すべて	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(あさり:みそ汁一人前)(その他:寿司ネタで2個分) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
13	魚のたまご (たらこ、半個)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(いくら、寿司ネタで2個分)(他、たらこ半個分程度) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
14	佃煮類 (海苔佃煮を除く)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(大さじ軽く1杯) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
15	塩辛類	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(大さじ軽く1杯) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			

たまご

1	鶏卵(中1個)	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	うずら卵(6個：50g) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			

豆類

1	とうふ	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(3分の1丁) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
2	揚げだし豆腐	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(4分の1丁)・厚揚げ(半個)・がんもどき(100g)・油揚げ(大1枚)など豆製品 ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
3	納豆	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(1人前：1パック) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
4	大豆、その他の豆の煮物や金時豆、お多福豆など甘い煮豆	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(小鉢に1杯、40g) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
5	落花生	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(10個程度)(ピーナッツ・バターピーナッツを含む) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			
6	落花生以外のナッツ類	毎日2回以上	毎日1回	週4～6回	週2～3回	週1回	月2～3回	月1回	食べなかった
	(軽くひと握り) ⇨	5割まで	2～3割減	同じくらい	2～3割増し	5割増し以上			