

Comparative study of the correlation between atherosclerosis and osteoporosis in women in Japan and Mongolia

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Abstract

Objective: Associations between vascular calcification and osteoporosis are well documented, yet effects of lifestyle on atherosclerosis and osteoporosis remain unclear. This study evaluated the relationship between atherosclerosis and osteoporosis of people with different lifestyles living on Uku Island in Japan (rice consumption and fishing lifestyle) and in Ulaanbaatar in Mongolia (meat consumption and nomadic lifestyle), and investigated the differences of lifestyles on atherosclerosis and osteoporosis.

Methods: Participants were women aged over 50 years who had undergone a previous medical examination for atherosclerosis and osteoporosis (Uku Island, 104, Ulaanbaatar, 71). Lifestyle habits were obtained by questionnaire. Bone mineral density of the right calcaneus was measured using quantitative ultrasound. Brachial-ankle pulse wave velocity was measured as an index of atherosclerosis.

Results: There were no significant differences in bone mineral density and brachial-ankle pulse wave velocity between the two groups, even though meat and dairy intake, number of meals skipped, and number of children were significantly greater in participants from Ulaanbaatar compared with Uku Island. Brachial-ankle pulse wave velocity showed significant positive correlations with age, systolic and diastolic blood pressures, and body mass index and a significant negative correlation with bone mineral density for both groups. With step-wise multiple regression analysis, brachial-ankle pulse wave velocity significantly correlated with age and bone mineral density for both populations. Systolic blood pressure significantly correlated with brachial-ankle pulse wave velocity for the Ulaanbaatar group.

Conclusions: Despite significant lifestyle differences, similar relationships between atherosclerosis and osteoporosis were observed in women from Uku Island and Ulaanbaatar. Hypertension was a significant contributing factor for atherosclerosis for the Ulaanbaatar group.

KEYWORDS

arterial stiffness, bone mineral density, lifestyle, Ulaanbaatar, Uku Island

1 | INTRODUCTION

Atherosclerosis and osteoporosis progress with age and become high-risk factors for cardiovascular disease and bone fractures, especially in postmenopausal women.^{1,2} In recent years, osteoporosis in postmenopausal women has been reported as a risk factor for coronary artery disease,³ and several studies have shown a negative correlation between bone mineral density (BMD) and degrees of vascular calcification.³⁻¹⁷ Although atherosclerosis and osteoporosis are influenced by lifestyle factors, there are no direct comparative studies on the relationship between atherosclerosis and osteoporosis in countries with different lifestyles.

In this study, we investigated the differences of lifestyle factors on the associations between atherosclerosis and osteoporosis by comparing a population from Uku Island, part of Sasebo in Nagasaki, Japan (typically rice and fish consumption) with a population from Ulaanbaatar, the capital city of Mongolia (typically meat and dairy consumption).

2 | MATERIALS AND METHODS

2.1 | Participants

The Seiwakai Medical Corp. previously carried out medical examinations for atherosclerosis and osteoporosis as a social contribution at Uku Island and Ulaanbaatar, where medical resources in these poorer areas are lacking. Participants of the medical examinations were recruited by circular notice for Uku Island and by radio broadcast for Ulaanbaatar. The total numbers of respondents were 172 from Uku Island in 2010, 2011, and 2012, and 75 from Ulaanbaatar in 2011. Participants in the study were women over the age of 50 years. Three women under the age of 50 years and 31 male individuals were excluded from analysis in the Uku Island group. Two female individuals under the age of 50 years and two male individuals were excluded from analysis in the Ulaanbaatar group. If a participant had received more than one medical examination, only data from the first examination were used (18 participants were twice examinees, and eight participants were three times examinees). The total numbers of participants included for analysis were 104 from Uku Island and 71 from Ulaanbaatar. The 104 participants in the Uku Island group were 8.8% of all female individuals over the age of 50 years and 5.7% of all female individuals from Uku Island. The 71 participants in the Ulaanbaatar group were about 0.12% of all female individuals over the age of 50 years from Ulaanbaatar.

2.2 | Medical examinations

Medical examinations were carried out at clinics on one day in summer in both countries.

2.3 | Measurement of lifestyle habits

A lifestyle habit survey was conducted using a 10-item questionnaire. The questionnaire gathered data about age, gender, height, body

weight, alcohol intake, meat intake, dairy intake, time spent sunbathing, number of meals skipped, and number of children. Survey questions were answered in writing just prior to the medical examination. The total numbers of questionnaires were 81 for Uku Island and 71 for Ulaanbaatar because the questionnaire was not conducted in 2011 for Uku Island participants. Alcohol, meat, and dairy intake were evaluated as the number of cups or dishes consumed per week. Number of skipped meals was the total number of meals skipped per week.

2.4 | Measurement of BMD

BMD of the right calcaneus was measured using a quantitative ultrasound measurement device (A-1000 Express/InSight; GE Healthcare Japan, Tokyo, Japan). The stiffness index was used as a parameter of BMD and was determined using the following equation:

$$\text{stiffness index} = 0.67 \times (\text{broadband ultrasound attenuation}) + 0.28 \times (\text{speed of sound}) - 420.$$
^{18,19} A figure of 70% or less than the mean stiffness index for BMD for a young adult was determined as osteoporosis.

2.5 | Measurement of brachial-ankle pulse wave velocity and blood pressure

Participants underwent brachial-ankle pulse wave velocity (baPWV) measurement as an index for atherosclerosis using a BP-203RPE2 (Omron-Colin, Tokyo, Japan) and a previously described method.²⁰ Participants were examined while resting in the supine position. Electrocardiographic electrodes were placed on both wrists, and cuffs were wrapped on both brachia and ankles. Pulse volume waveform at each brachium and ankle was recorded by a semiconductor pressure sensor. BaPWV was measured after at least 5-minute rest. The standard value of baPWV is 1400 cm/s. BaPWV exceeding 1400 cm/s is determined as atherosclerosis, and there is increased risk for cerebral vascular disease and cardiovascular disease. Blood pressure is used the value of measurement of right upper arm obtained during baPWV measurement.

2.6 | Ethical considerations

This study was conducted in accordance with the Helsinki declaration and ethical guidelines of epidemiological studies. The study protocol was approved by the Ethics Committee of Muta Hospital. Direct informed consent was not sought from the individual participants, because the collection of data was obtained during usual health examination. All data analyses were conducted in a confidential manner. Participant identities were anonymous.

2.7 | Statistical analysis

Data are expressed as mean±standard deviation. Simple linear regression analysis was performed to evaluate associations between baPWV and the other variables. Step-wise multiple regression

TABLE 1 Clinical characteristics of the participants

	Uku Island	Ulaanbaatar	P-value
Number	104	71	
Age (y)	71.8±9.1	67.9±8.4	.0049
BMI (kg/m ²)	23.4±3.9	27.0±5.6	.0001
SBP (mm Hg)	144.0±19.2	150.8±26.2	.0649
DBP (mm Hg)	80.2±9.9	85.9±14.1	.0039
Rt.baPWV (cm/s)	1935±556	1932±573	.9681
Lt.baPWV (cm/s)	1973±624	1949±570	.7942
Stiffness index of BMD (%YAM)	68.2±17.9	66.3±14.0	.4571
Lifestyle habits			
Number	81	71	
Intake of meat	1.45±1.83	7.39±3.19	<.0001
Intake of dairy products	7.95±6.79	17.1±11.5	<.0001
Number of children	2.93±1.61	5.16±2.69	<.0001
Number of meals skipped	0.095±0.48	1.42±2.33	.0001
Alcohol consumption	0.121±0.72	0.163±0.65	.7332

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMD, bone mineral density; YAM, young adult mean; baPWV, brachial-ankle pulse wave velocity.

The total number of questionnaires was 81 for Uku Island and 71 for Ulaanbaatar. No part of any answer was left blank. Alcohol, meat, and dairy intake were evaluated as the number of cups or dishes consumed per week. For dairy products, if a participant consumed more than one, the sum total was used for evaluation. Number of skipped meals was the total number of meals skipped per week.

analysis was performed in the forward selection to determine correlations between baPWV and each independent variable. Statistical analysis was performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). A P-value <.05 was considered statistically significant.

3 | RESULTS

3.1 | Clinical characteristics of participants

Table 1 summarizes the participants' clinical parameters. Participants were relatively old (71.8±9.1 years old in the Uku Island group and 67.9±8.4 years old in the Ulaanbaatar group). Uku Island participants were significantly older than Ulaanbaatar participants ($P=.0049$). Uku Island participants had significantly lower body mass index (BMI) than Ulaanbaatar participants (23.4±3.9 kg/m² for Uku Island and 27.0±5.6 kg/m² for Ulaanbaatar; $P=.0001$). Uku Island participants had significantly lower diastolic blood pressure than Ulaanbaatar participants (80.2±9.9 mm Hg for Uku Island and 85.9±14.1 mm Hg for Ulaanbaatar; $P=.0039$). Mean baPWV was high for women from both groups (right baPWV: 1935±556

and left baPWV: 1973±624 for Uku Island; right baPWV: 1932±573 and left baPWV: 1949±570 for Ulaanbaatar), indicating atherosclerosis.

Mean stiffness index of BMD was low for women from both groups (68.2±17.9 for Uku Island and 66.3±14.0 for Ulaanbaatar), indicating osteoporosis.² No significant differences in baPWV and stiffness index of BMD were observed between Uku Island and Ulaanbaatar participants.

For lifestyle habits, Ulaanbaatar participants had significantly more meat and significantly more dairy intake compared with Uku Island participants (meat consumption: 1.45±1.83 for Uku Island and 7.39±3.19 for Ulaanbaatar; $P<.0001$) (dairy consumption: 7.95±6.79 for Uku Island and 17.1±11.5 for Ulaanbaatar; $P<.0001$). Number of children and number of meals skipped were significantly greater in the Ulaanbaatar group than the Uku Island group (number of children: 2.93±1.61 for Uku Island and 5.16±2.69 for Ulaanbaatar; $P<.0001$) (number of meals skipped: 0.095±0.48 for Uku Island and 1.42±2.33 for Ulaanbaatar; $P=.0001$).

There was no significant difference in alcohol intake between groups.

3.2 | Correlation between baPWV and clinical variables

Simple linear regression analysis was performed between baPWV and clinical variables. BaPWV showed a significant positive correlation with age ($r=.555$, $P=.0001$ in the Uku Island group and $r=.589$, $P=.0001$ in the Ulaanbaatar group), systolic blood pressure ($r=.505$, $P=.0001$ in the Uku Island group and $r=.634$, $P=.0001$ in the Ulaanbaatar group), and diastolic blood pressure ($r=.337$, $P=.0001$ in the Uku Island group and $r=.478$, $P=.0001$ in the Ulaanbaatar group), and a significant negative correlation with BMD ($r=-.417$, $P=.0001$ in the Uku Island group and $r=-.414$, $P=.0001$ in the Ulaanbaatar group) and BMI ($r=-.247$, $P=.010$ in the Uku Island group and $r=-.313$, $P=.009$ in the Ulaanbaatar group).

3.3 | Associations between baPWV and BMD

Figure 1 shows the correlation between baPWV and stiffness index of BMD. BaPWV showed a significant negative correlation with stiffness index of BMD for both the Uku Island group ($r=-.417$, $P=.0001$) and the Ulaanbaatar group ($r=-.414$, $P=.0001$). Figure 2 shows mean baPWV values by quartiles of stiffness index of BMD.

Participants were stratified into four groups by different bone density (lowest stiffness, low stiffness, high stiffness, and highest stiffness index of BMD by quartile). BaPWV was highest in participants of the lowest stiffness index of BMD group in both Uku Island participants ($P=.049$ vs. participants with low BMD quartile, $P=.016$ vs. participants with high BMD quartile, $P<.0001$ vs. participants with highest BMD quartile) and Ulaanbaatar participants ($P=.4830$ vs. participants with low BMD quartile, $P=.096$ vs. participants with high BMD quartile, $P=.013$ vs. participants with highest BMD quartile).

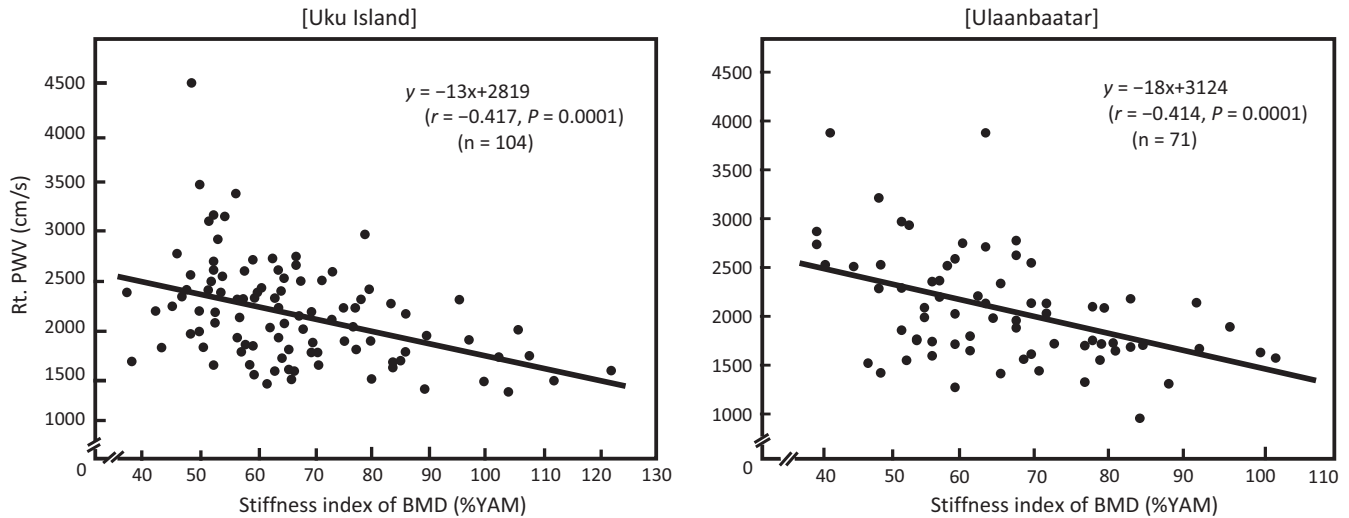


FIGURE 1 Correlation between brachial-ankle pulse wave velocity (baPWV) and stiffness index of bone mineral density (BMD)

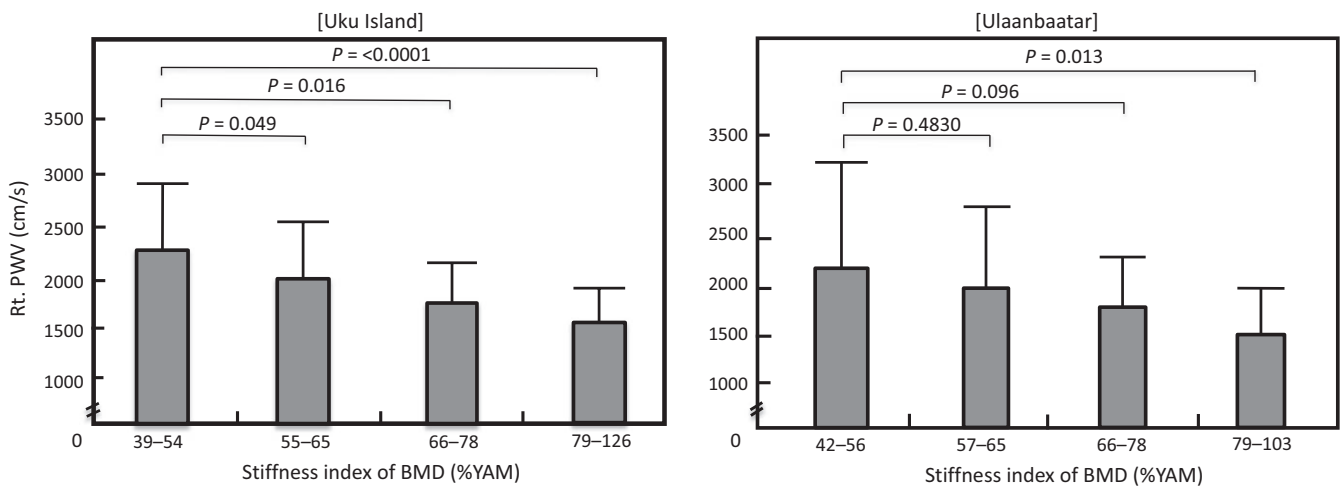


FIGURE 2 Mean values of brachial-ankle pulse wave velocity (baPWV) by quartiles of stiffness index of bone mineral density (BMD)

3.4 | Assessment of factors related to baPWV

Table 2 shows the results of step-wise multiple regression analysis between baPWV and clinical variables. Step-wise regression analysis was performed for variables that showed significant correlations with baPWV following linear regression analysis in both groups. Stiffness index of BMD was found to be an independent predictor for baPWV in both Uku Island ($P=.0339$) and Ulaanbaatar ($P=.0469$) participants. Age showed a stronger correlation with baPWV than stiffness index of BMD in both populations ($P=.0001$ for Uku Island and $P=.0001$ for Ulaanbaatar). Participants from Ulaanbaatar showed a significant correlation with systolic blood pressure ($P=.0001$).

4 | DISCUSSION

To the best of the authors' knowledge, this is the first comparative study examining the relationship between atherosclerosis and

osteoporosis in two Asian populations, these being Uku Island in Japan and Ulaanbaatar in Mongolia, with different lifestyles using the same measurement device.

The mechanism behind the relationship between atherosclerosis and osteoporosis is considered to be increased production of the inflammatory cytokines²¹ tumor necrosis factor- α and interleukin-1 β with increased oxidative stress because of aging and decreased production of sex hormones because of menopause. This increased production results in increased levels of receptor activator of nuclear factor kappa β ligand (RANKL), which may participate in both bone loss and vascular calcification, resulting in a shift of calcium from bone to the vessel wall.²²

Chronic inflammation and calcium metabolism are considered to be influenced by lifestyle habits. In the current study, we found that meat and dairy intake and the number of children and skipped meals were significantly greater in participants from Ulaanbaatar compared with participants from Uku Island. There was, however, no significant difference in BMD and baPWV between the two groups.

TABLE 2 Identification of contributing factors to baPWV using multiple regression analysis and the step-wise method

Uku Island	$R^2=0.51$			
	B coefficient	SE	t-value	P-value
Age (y)	21.873	5.899	3.708	.0001
Stiffness index of BMD (%YAM)	-6.328	2.947	-2.147	.0339
SBP (mm Hg)	6.435	3.489	1.845	.0683
Ulaanbaatar	$R^2=0.61$			
	B coefficient	SE	t-value	P-value
Age (y)	26.671	7.052	3.782	.0001
Stiffness index of BMD (%YAM)	-8.834	4.358	-2.027	.0469
SBP (mm Hg)	10.762	2.773	3.882	.0001

baPWV, brachial-ankle pulse wave velocity; BMD, bone mineral density; SBP, systolic blood pressure; BMI, body mass index. Objective variable: baPWV; Explanatory variables: age, stiffness index of BMD, SBP, and BMI.

Increased meat intake results in an excessive intake of protein. Diets high in protein are thought to increase urinary calcium,^{23,24} and acidifying amino acids released after protein digestion can stimulate osteoclastic bone resorption, thereby reducing BMD. An increased frequency in dairy intake was reported to provide a preventive effect from osteoporosis.²⁵ Additionally, the number of live births has been reported as an independent risk factor for osteoporosis.²⁶ Skipping meals has been reported to have a negative correlation with BMD.²⁷ Participants from Ulaanbaatar were found to have both positive (dairy intake) and negative contributing factors (meat intake, number of children, and skipping meals) compared with participants from Uku Island for effects on BMD. From these positive and negative contributing factors, it is possible that BMD of participants from Ulaanbaatar might not be significantly higher than that of participants from Uku Island, even though Ulaanbaatar participants were significantly younger and had higher BMI than participants from Uku Island.

Meat consumption²⁸ and intake of whole-fat dairy²⁹ have been reported to show a positive correlation with pulse wave velocity. Women who had given birth naturally have been reported to have a significantly lower pulse wave velocity.³⁰ Skipping meals has been reported to be a possible risk factor for metabolic syndrome.³¹ In the current study, participants from Ulaanbaatar were found to have positive (meat intake, dairy intake, and number of meals skipped) and negative (number of children) contributing factors compared with participants from Uku Island for effects on baPWV. From these positive and negative contributing factors, the baPWV of participants from Ulaanbaatar might not be significantly lower than that of participants from Uku Island.

We found a significantly negative correlation between baPWV and BMD in participants from both Ulaanbaatar and Uku Island. From results of step-wise multiple regression analysis, BMD and age were identified as factors contributing significantly to baPWV in both groups.

Systolic blood pressure was only a contributing factor to baPWV in the Ulaanbaatar group. Hypertension among Mongolian people has been reported to be influenced by body weight, high salt intake,

smoking, and high serum cholesterol levels.³² Mongolian people have been reported to have a higher salt intake than people from Sasebo.^{33,34} It is possible that the high salt intake in Mongolian people contributed to the observed differences in results in the current study.

An advantage of the current study is that all measurements were performed using the same method and type of device. This is important for comparative studies between populations from different countries.

This study had several limitations. First, we were unable to take blood samples for measurement of parameters considered to influence atherosclerosis and osteoporosis, such as serum levels of cholesterol, blood glucose, and sex hormones. BMI in Ulaanbaatar participants was high (27.0 ± 5.6); therefore, there is the possibility that some participants had hyperlipidemia and diabetes mellitus. Second, some data about lifestyle habit and effect on BMD and baPWV were absent, such as smoking habit, amount of exercise, and information on medication for hypertension and osteoporosis. It is possible that other contributing factors might have had an effect on BMD and baPWV in both groups. Third, we used ultrasound to measure BMD. Ultrasound is portable, quick, and noninvasive. Ultrasound is very useful for medical examinations in the field and makes it possible to compare BMD in different countries easily. Generally, BMD should be measured by dual-energy X-ray absorptiometry in clinical settings. However, a previous study demonstrated that BMD measured using ultrasound was significantly comparable to BMD measured using dual-energy X-ray absorptiometry.³⁵ Finally, it must be considered with the presence of selection bias. In this recruiting method in both countries, there was possibility that was collected high health awareness group.

5 | CONCLUSION

Lifestyle habits between Ulaanbaatar and Uku Island participants were significantly different, yet there were no significant differences in baPWV and BMD. Positive and negative contributing factors from different lifestyle behaviors, which influence osteoporosis and

atherosclerosis, were not found to be significantly different in these study populations from Uku Island and Ulaanbaatar. We found the same negative relationship between baPWV and BMD in both study groups. Hypertension was a significant contributing factor for atherosclerosis in Ulaanbaatar participants, but not in Uku Island participants.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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