**Cross-Sectional Association of Bone Mineral Density with Coronary Artery Calcification in Multi-Ethnic Middle-Aged Men ERA JUMP Study**

by

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**Abstract**

**Background:** Osteoporosis and coronary artery disease (CAD) are common diseases. Low bone mineral density (BMD) leads to osteoporosis and fractures. CAD is the leading cause of death in the US and the world. Coronary artery calcification (CAC) is a significant and independent predictor of future cardiovascular events. Some studies have revealed the inverse association between BMD and CAD in women. However, the evidence of the relationship is controversial in men, and little evidence exists in multi-ethnic middle-aged men. We hypothesized that there is a significant inverse association of BMD with CAC in middle-aged men.

**Methods:** ERA JUMP study was a population-based study of 1,134 men aged 40 to 49 (267 Caucasians, 84 African Americans, 242 Japanese Americans, 308 Japanese, and 233 Koreans). The participants were examined for CAC, cardiovascular risk and other factors. CAC and the mean Hounsfield Unit value of vertebral bone (a surrogate for bone density) were studied using electron-beam computed tomography. CACs were quantified with the Agatston method. Vertebral bone density (VBD) was quantified by computing the mean HU value in manually outlined region of the T12 to L3 vertebrae. Robust linear regression and multiple logistic regression analyses were performed.

**Results:** The mean VBD was 175.4 HU (standard deviation: 36.3 HU), the median of the CAC score was 0 (Interquartile range: (0, 4.5)), and the prevalence of CAC was 19.0%. VBD was significantly associated with CAC using robust linear regression (β=-0.2069, p-value=0.005). After adjusting for traditional cardiovascular risk factors, the relationship remained statistically significant (β=-0.1849, p-value=0.011). In logistic regression, the odds ratio (OR) of the presence of CAC for a one-unit increase in VBD was 0.9926 (95% CI: 0.9884-0.9969, p-value=0.001). The association persisted after adjusting for the same set of covariates (OR: 0.9950 95% CI: 0.9902-0.9999, p-value=0.045).

**Conclusions:** There was a significant inverse association of our VBD surrogate with CAC in multi-ethnic middle-aged men. This study’s public health importance lies in the probability of the presence of common pathologies between BMD and CAC in multi-ethnic middle-aged men, which may lead to the development of new screening methods and treatments for osteoporosis and CAD in middle-aged men.

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Preface

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# Introduction

Osteoporosis is a common disease with a prevalence of 5.1% in men aged 65 and over and 24.5% in women aged 65 and over in the US [1]. Low bone mineral density (BMD) leads to osteoporosis and fragility fractures, and BMD decreases with age [2]. Osteoporotic fractures predominantly occur at the hip and spine, which result in long-term functional impairments, bedridden status and death [3]. The 10-year probability of major osteoporotic fracture is 5.3% for adults aged 40 and over [4], and it is reported that hip fracture are associated with mortality during the first year after fracture ranging from 8.4% to 36% [5]. Heart disease including coronary artery disease (CAD) is the leading cause of death [6]. An estimated 16.5 million Americans aged 20 and over have CAD [6], and about 370,000 Americans die of CAD [7]. Thus, it is important to detect CAD and osteoporosis and start treatment for CAD and osteoporosis at an early stage. Vertebral bone density (VBD) depicted on CT images is a surrogate marker of BMD and correlates with BMD measured on dual-energy X-ray absorptiometry (DEXA) [8] [9].Coronary artery calcification (CAC) is also a well-established biomarker of coronary atherosclerosis and is a significant predictor of the myocardial infarction and cardiovascular event independent of traditional risk factors [10].

Some articles have reported the association of BMD with CAC, vascular calcification or atherosclerosis. However, low BMD has been associated inconsistently with vascular calcification or atherosclerosis especially in men who have a lower prevalence rate of osteopenia and osteoporosis. A retrospective study in 209 patients (mean age: 67 years, 89% women) reported that a risk of coronary artery stenosis >50% was higher in the group with osteoporosis (OR: 5.6, p-value<0.0001) [11]. In the study that assessed 5,590 consecutive subjects who underwent CAC scanning and thoracic BMD measurement (mean age: 57 years, and 69% men), there was an inverse relationship between CAC and VBD assessed by computed tomography (CT) in both genders [12]. However, another study reported that there was no significant association of low BMD with angiographically determined coronary atherosclerosis in 623 men (mean age: 64 years) [13]. A longitudinal study revealed that a decrease in BMD was associated with an increase in CAC in elderly women but not in men [14]. Also, the Framingham Heart Study including 364 women and 190 men showed that a decrease in BMD in the metacarpal relative cortical area was associated with an increase in the aortic calcification index in women after controlling for all potential confounders (p-value=0.01), but there was no association in men (p-value=0.50) [15].

Most studies analyzing the association of BMD with CAC target Caucasians. On the other hand, it was reported that African Americans have a higher BMD than Caucasians [2], and the age-adjusted prevalence of osteoporosis at the femur neck or lumbar spine was higher in Asians and lower in African Americans compared to Caucasians [16]. The evidence of the relationship between low BMD and CAC is controversial in men, and there is no previous study that has examined the relationship in middle-aged men including Caucasians, African Americans, Japanese Americans, Japanese and Koreans [17]. We hypothesized that the multi-ethnic middle-aged men with lower BMD would have a higher CAC or a higher prevalence of CAC. We investigated whether VBD assessed on CT images is associated with CAC in men aged 40 to 49 including Caucasians, African Americans, Japanese Americans, Japanese and Koreans.

# Methods

## Study Population

The ERA JUMP study was used to analyze the association of BMD with CAC. The study population has been described in detail elsewhere [18]. Briefly, between 2002 and 2006 population-based samples of men aged 40 to 49 were randomly selected and consisted of: (1) Caucasian men and African American men from the voter registration list of Allegheny County, US, (2) Japanese American men from lists of offspring of Japanese American fathers who participated in the Honolulu Heart Program in Hawaii, US, (3) Japanese men from the Basic Residents’ Register of Kusatsu, Japan, and (4) Korean men from Ansan, Gyeonggi-do, South Korea.

All participants were without clinical cardiovascular disease, type 1 diabetes, cancer except skin cancer in the past 2 years, renal failure, and genetic familial hyperlipidemias. We excluded those with missing data (n=198) and fractures of the lumber spine (n=3), and our final sample was 1,134 men (267 Caucasians, 84 African Americans, 242 Japanese Americans, 308 Japanese, and 233 Koreans). The study was approved by the Institutional Review Boards of Shiga University of Medical Science, Otsu, Japan; University of Pittsburgh, Pittsburgh, Pennsylvania, US; Kuakini Medical Center, Honolulu, Hawaii; and Korea University, Seoul, South Korea. All participants provided written informed consent.

## Vertebral Bone Assessment

Non-contrast CT examinations were performed using electron-beam computed tomography (EBCT) using GE-Imatron C150 EBT scanners (GE Medical Systems, South San Francisco, US) at the four centers using standardized CT protocols. Scanners were calibrated regularly by technicians during normal operation. The CT image data was acquired at an exposure between 125 to 35 mAs. The CT images were reconstructed using either the “sharp” or “standard” kernels at a 6.0 mm thickness and interval. Subjects were scanned from the aortic arch to the iliac bifurcation. A single reader manually outlined an ellipsoidal region of interest (ROI) on the central portion of the thoracic and lumbar vertebrae (T12 to L3) depicted on the CT images, which was based on a previously validated approach [19] [20]. Cortical bone and calcification within the vertebra were excluded. Subjects without T12 to L3 vertebrae completely depicted on the CT images were excluded from the study. The mean HU value across the four vertebral ROIs was computed as a surrogate for and will be referred to in this study as VBD. The reader was blinded to the subjects’ characteristics. The vertebrae of 60 subjects were re-analyzed a minimum of 3 weeks after the initial assessment to evaluate intra-reader agreement. Intra-reader agreement between the first and second analyses was very high (concordance correlation coefficient of 0.996).

## CAC Measurement

The Agatston method was used to assess CAC depicted on the EBCT images using AccuImage software (AccuImage Diagnostics, South San Francisco, CA, US) [21]. Subjects were scanned from the aortic root to the apex of the heart to evaluate CAC with contiguous images reconstructed at a 3.0 mm thickness and interval. A single experienced reader at the Cardiovascular Institute, University of Pittsburgh, Pennsylvania, read and assessed the coronary scans from all four centers. The reader was blinded to the subjects’ characteristics. The reproducibility of the coronary scans was very high (intraclass correlation of 0.98) [22]. The cut-off point of the CAC score ≥10 Agatston units was used to deﬁne the presence (or absence) of CAC, as previously reported [23] [24].

## Other Measurements

A self-administered questionnaire was used to obtain information from participants on demography, smoking habits, alcohol use, medications (hypertension, dyslipidemia, and diabetes mellitus), and medical history. Current smoking was defined as smoking cigarettes over the past month. Alcohol use was defined as alcohol consumption at least two days per week.

Body-mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Blood pressure (BP) was measured in the right arm of the seated participant after the participant sat quietly for five minutes, using an appropriate-sized cuff, with an automated sphygmomanometer (BP-8800, Omron Health Care Co. Ltd, Tokyo, Japan). The average of 2 measurements was used to determine BP. Hypertension was defined as systolic BP ≥140 mmHg, diastolic BP ≥90 mmHg, or use of anti-hypertensive medication. Diabetes mellitus was defined as a fasting blood glucose ≥7.0 mmol/L or use of anti-diabetic medication. Total cholesterol and triglycerides were measured using enzymatic assays, and high-density lipoprotein cholesterol (HDL-C) was measured using a direct method. LDL-C was estimated using Friedewald’s formula [7]. When triglycerides exceeded 400 mg/dl, we did not estimate LDL-C and measured LDL-C directly. Lipid measurements were standardized according to the protocol for the US Centers for Disease Control and Prevention/Cholesterol Reference Method Laboratory Network. Hyperlipidemia was defined as triglycerides >150 mg/dl, HDL-C <40 mg/dl, LDL-C >140 mg/dl, or use of anti-hyperlipidemia medication.

## Statistical Analyses

Participant characteristics were shown as means and standard deviations (SDs) for continuous variables with normal distributions, medians and interquartile ranges (IQRs) for continuous variables with skewed distributions, and frequencies and percentages for categorical variables. The CACs were used as continuous and binary variables which were divided into two groups: CAC score was <10 or >10. To examine the differences of the CAC score and the prevalence of CAC >10 among VBD quartiles, a nonparametric test for trend in STATA software (version 14, Stata Corporation, College Station, Texas) across ordered groups was used.

To examine multivariable-adjusted associations of CAC with VBD, we used robust linear and logistic regressions because the distribution of the CAC score was highly skewed. For a logistic regression, we chose a cutoff point of the CAC score of 10. For multivariable adjustments in robust linear and logistic regressions, we first adjusted for age, race, and BMI (Model 1), then further adjusted for hypertension, diabetes, and hyperlipidemia (Model 2). In Model 3, we additionally adjusted for alcohol use and smoking status (current, past, or never smokers). Two-tailed p-values of <0.05 were considered to indicate statistical significance. All these statistical analyses were performed with STATA software.

# Results

The mean age was approximately 45 years, and the mean (SD) BMI was 25.9 (4.1) (Table 1). The prevalence of hypertension, diabetes, and hyperlipidemia was 22.4%, 7.1%, and 68.9%, respectively. The smoking status for never, former, and current was 45.2%, 27.7%, and 27.2%, respectively. The percentage of alcohol use was 49.0%. The median CAC (IQR) was 0 (0, 4.5), and the prevalence of CAC was 19.0%. The mean (SD) HU value of the vertebral bone ROIs was 175.4 (36.3) HU. The VBD in African Americans was higher and VBD in Japanese was lower than in Caucasians (Table B1).

The prevalence of CAC (CAC score ≥10) significantly decreased across increasing quartiles of VBD (p-value=0.004) (Table 2). The ranges of VBD in quartiles 1 through 4 were 61.4-151.6 HU, 151.6-175.35 HU, 175.35-196.9 HU, and 196.9-325.8 HU, respectively. The prevalence of CAC for the quartiles was 25.2%, 19.0%, 15.6%, and 16.2%, respectively. The median CAC score for the quartiles (IQR) was 0 (0, 10.3), 0 (0, 4.1), 0 (0, 4.4), and 0 (0, 3.8), respectively. No signiﬁcant trend existed across the quartiles for the CAC score.

The VBD was significantly associated with the CAC score in the unadjusted model (β=-0.2069, p-value=0.005) (Table 3). The relationship of VBD and CAC remained statistically significant, adjusting for age, race, BMI, prevalence of hypertension, hyperlipidemia, and diabetes, alcohol use, and smoking (β=-0.1849, p-value=0.011). In the unadjusted model, the odds ratio (OR) of the presence of CAC for a one-unit increase in VBD was 0.9926 (95% CI: 0.9884-0.9969, p-value=0·001), and the odds of the presence of CAC were 7.12% lower with a 10 unit increase in VBD (Table 4). The signiﬁcant association between VBD and the presence of CAC persisted after adjusting for covariates (OR: 0.9950, 95% CI: 0.9902-0.9999, p-value=0·045), and the odds of the presence of CAC were 4.86% lower with a 10 unit increase in VBD. There was no significant relationship between VBD quartiles and the presence of CAC in the logistic regression.

# Discussion

In our all male cohort, we observed a significant inverse relation between our surrogate for VBD and the prevalence of CAC, and that there was a significant association of low VBD with the degree and presence of CAC in middle-aged men, adjusting for traditional risk factors for CAC. This is the first study to report the association of low VBD with CAC in middle-aged men internationally.

Our finding of an association between CAC and VBD, a surrogate for overall BMD, suggests that there may be common pathologies between BMD and CAC in multi-ethnic middle-aged men. Many studies have shown the significant inverse relationship between BMD and CAC or atherosclerosis, especially in postmenopausal women. A systematic review and meta-analysis involving 25 studies and 10,299 subjects (mean ages: 55 to 77 years) showed that the incidence of atherosclerotic vascular abnormalities was significantly increased in low BMD patients, compared to patients with normal BMD (OR: 1.81, 95% CI: 1.01-2.19, p-value<0.00001), and the association was stronger in postmenopausal women (OR: 2.23, 95% CI: 1.72-2.89, p-value<0.00001) [17]. Ahmadi, N. et al. showed a strong inverse association of VBD with CAC in postmenopausal women. (OR: 4.89 in CAC=101-400, OR: 8.32 in CAC=400+ vs. CAC=0) [12]. Another cross-sectional study revealed that BMD was strongly related to multidetector CT measures of CAC (mean CAC score was 43.2±89.9 in normal status, 126.9±180.3 in osteoporosis, and 198.2±301.2 in osteopenia at the femoral neck, p-value<0.05) [25]. A longitudinal study that also showed postmenopausal women in the highest quartile for gains in aortic calcification had four times greater yearly bone loss (5.3 vs.1.3% yearly, p-value<0.001) than women of similar age in the lowest quartile [26]. While these studies have shown a significant inverse relationship between BMD and CAC, this association is usually strongest in women.

Our study showed a significant association of low VBD with CAC in middle-aged men, while previous studies examining BMD and CAC have reported inconsistent results in men. This inconsistency may be due to differences in race distribution among the various studies. The significant association of low BMD with CAC in previous studies was primarily observed in people who have lower BMD or higher risks for osteopenia and osteoporosis, such as Asians who have higher risk for osteopenia and osteoporosis and comprised nearly 70% of our study cohort [12] [16]. Consistent with previous studies [2] [16], African Americans had significantly higher BMD and Japanese had significantly lower BMD compared to Caucasians in our study (Supplement Table B1). Ahmadi, N., et al. [12] showed in 5,590 subjects, including Asian and African American men, that VBD in African Americans was the higher, and VBD in Caucasians and Asians were lower than in Hispanics, and they reported the inverse relationship between VBD and CAC. On the other hand, Beer, S., et al. [13] and Campos-Obando, N., et al. [14] investigated the association of BMD with CAC only in Caucasian men and reported no significant relationship between BMD and CAC.

There are common factors related to BMD and CAC that may explain our findings. First, overlapping inflammatory processes affects both BMD and vascular calcification. Higher serum levels of inflammatory markers, such as C-reactive protein (CRP), interleukin (IL)-6, and tumor necrotizing factor α (TNF-α), and oxidative stress are associated with the severity of atherosclerosis and vascular calcification [27] [28] [29] [30]. IL-6 and TNFα are produced in the vessel wall by the endothelial cells, smooth muscle cells, and macrophages, which leads to recruitment of macrophages and monocytes to form calcifications [29] [31]. Inflammatory mediators, such as CRP, IL-6, and TNF-α, and oxidative stress likewise play an important role in osteoclast function, bone turnover, and bone remodelling by stimulating osteoclast differentiation and the progression of osteoporosis [32] [33] [34] and the progression of osteoporosis. In our study, CRP and other inflammatory factors were not measured in all participants, but when we analyzed the relationship of BMD and CAC and added CRP to the model, the significant relationship remained (data not shown). In addition, several bone matrix proteins, including matrix Gla protein (MGP), osteoprotegerin (OPG), osteopontin (OPN), osteonectin (ON), bone morphogenetic protein (BMP)-2, collagen I,osteocalcin (OC), receptor-activated nuclear factor-kappa B ligand (RANKL), and the mineral hydroxyapatite, are also present in atherosclerotic arteries [17]. Age, smoking status, and physical inactivity are modifiable risk factors for both CAD and bone loss [30] [35]. Parathyroid hormone is reported as a predictor for both vascular calcification and bone turnover [30] [36], and estrogen deprivation after menopause is a cause of osteoporosis and is related to the increasing incidence rate of cardiovascular diseases in women [35].

This is the ﬁrst large population-based study in middle-aged men that includes Caucasians, African Americans, Japanese Americans, Japanese, and Koreans to address the relation between VBD and CAC. Thus, we believe our results can be generalized to the general population.

There are also some limitations of the present study. First, our study only included men aged 40 to 49, and, therefore, our results may not be generalizable to women and men over 50 years old. However, the value of this study based on our cohort is that the incidence rate of cardiovascular disease in men is higher than women and atherosclerosis starts to progress in middle age. Second, since this study is a cross-sectional analysis, we cannot evaluate the causal relation between BMD and CAC or cardiovascular disease. Third, the study is observational and cannot exclude the possibility of residual confounding factors. We did not assess physical activity levels related to both BMD and CAC, which may impact the association. Finally, we used x-ray attenuation, which is represented in CT image pixel HU values as computed attenuation of four lower vertebrae as a surrogate for overall BMD. Although, x-ray attenuation is a reasonable surrogate for density, we only evaluate a small section of the skeletal anatomy, albeit a critical anatomical region related to BMD. There are other approaches (e.g., DEXA) that may have produced different results, but we believe that our approaches are sufficient to capture first order effects related to BMD and CAC.

In conclusion, our observations demonstrate an inverse relation between BMD and CAC in multi-ethnic middle-aged men in a large population-based cross-section study. This relation is not modiﬁed by other traditional risk factors for cardiovascular disease. In the future, longitudinal research for establishing the evidence of the relation in middle-aged men and further research for revealing the potential mechanisms and the racial difference of the association are warranted. Our finding suggests that there may be common pathologies between BMD and CAC in multi-ethnic middle-aged men, which may lead to the development of new screening methods and treatments for osteoporosis and CAD in middle-aged people to reduce the mortality related to osteoporosis and CAD.

* + - * 1. Tables

Table 1. Subjects Characteristics (n=1,134)

|  |  |
| --- | --- |
| Age (years) | 45.2 ± 2.8 |
| BMI (kg/m2) | 25.9 ± 4.1 |
| Race Caucasian, n (%) African American, n (%) Japanese American, n (%) Japanese, n (%) Korean, n (%) | 267 (23.5)84 (7.4)242 (21.3)308 (27.2)233 (20.6) |
| Smoking status |  |
|  Never, n (%) | 512 (45.2) |
|  Former, n (%) | 314 (27.7) |
|  Current, n (%) | 308 (27.2) |
| Alcohol use, n (%) | 556 (49.0) |
| Systolic blood pressure (mmHg) | 124.0 ± 14.0 |
| Medications for hypertension, n (%) | 111 (9.8) |
| Hypertension, n (%) | 254 (22.4) |
| Glucose | 105.1 ± 18.1 |
| Medications for diabetes, n (%) | 21 (1.9) |
| Diabetes, n (%) | 80 (7.1) |
| LDL-C (mg/dl) | 127.1 ± 34.9 |
| HDL-C (mg/dl) | 50.2 ± 13.5 |
| Total cholesterol (mg/dl) | 207.9 ± 37.9 |
| Triglyceride (mg/dl) | 131.5 (85.0, 190.0) |
| Medications for hyperlipidemia, n (%) | 105 (9.3) |
| Hyperlipidemia, n (%) | 781 (68.9) |
| CAC score | 0 (0, 4.5) |
| CAC score >10, n (%) | 215 (19.0) |
| Mean HU value from T12-L3 | 175.4 ± 36.3 |

The mean ± standard deviation is shown unless otherwise mentioned. The median (interquartile range) is shown in triglyceride and the CAC score. BMI = body-mass index; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; CAC = coronary artery calciﬁcation

Table 2. Association of Quartiles of VBD with CAC

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Quartile of Mean HU value | Q1(n=282) | Q2(n=285) | Q3(n=283) | Q4(n=284) | p-value for trend |
| Median CAC score (IQR) | 0 (0, 10.3) | 0 (0, 4.1) | 0 (0, 4.4) | 0 (0, 3.8) | 0.534 |
| CAC Score >10, n (%) | 71 (25.2) | 54 (19.0) | 44 (15.6) | 46 (16.2) | 0.004 |

Q1: 61.4-151.6, Q2: 151.6-175.35, Q3: 175.35-196.9, Q4: 196.9-325.8

VBD = Vertebral bone density; CAC = coronary artery calciﬁcation

Table 3. Association of VBD with CAC Score (Robust Linear Regression)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | β | 95%CI | p-value | R2 |
| Unadjusted | -0.2069 | (-0.3512, -0.0626) | 0.005 | 0.0083 |
| Model 1 | -0.2199 | (-0.3676, -0.0722) | 0.004 | 0.0468 |
| Model 2 | -0.2186 | (-0.3673, -0.0700) | 0.004 | 0.0499 |
| Model 3 | -0.1849 | (-0.3268, -0.0430) | 0.011 | 0.0602 |

Model 1: Vertebral bone attenuation + age, race, and BMI

Model 2: Model 1 + hypertension, hyperlipidemia, and diabetes

Model 3: Model 2 + alcohol and smoking

VBD = Vertebral bone density; CAC = coronary artery calciﬁcation

Table 4. Association of VBD with CAC >10 (Logistic Regression)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OR | 95%CI | p-value | Pseudo R2 |
| Unadjusted | 0.9926 | (0.9884, 0.9969) | 0.001 | 0.0108 |
| Model 1 | 0.9938 | (0.9892, 0.9985) | 0.010 | 0.1099 |
| Model 2 | 0.9937 | (0.9889, 0.9985) | 0.010 | 0.1248 |
| Model 3 | 0.9950 | (0.9902, 0.9999) | 0.045 | 0.1428 |

Model 1: Vertebral bone attenuation + age, race, and BMI

Model 2: Model 1 + hypertension, hyperlipidemia, and diabetes

Model 3: Model 2 + alcohol and smoking

VBD = Vertebral bone density; CAC = coronary artery calciﬁcation

* + - * 1. Supplemental Table

Table B1. Subjects Characteristics for Each Race

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | All(n=1,134) | Caucasian(n=267)  | African American(n=84) | Japanese American(n=242) | Japanese(n=308) | Korean(n=233) |
| Age (years) | 45.2 ± 2.8\*\* | 45.0 ± 2.8 | 45.0 ± 2.7 | 46.0 ± 2.9 | 45.1 ± 2.8 | 44.8 ± 2.8 |
| BMI (kg/m2) | 25.9 ± 4.1\*\* | 27.5 ± 4.0 | 29.5 ± 5.9 | 27.3 ± 3.9 | 23.7 ± 3.0 | 24.3 ± 2.4 |
| Smoking status | \*\* |  |  |  |  |  |
|  Never, n (%) | 512 (45.2) | 197 (73.8) | 45 (53.6) | 158 (65.3) | 53 (17.2) | 59 (25.3) |
|  Former, n (%) | 314 (27.7) | 52 (19.5) | 15 (17.9) | 55 (22.7) | 105 (34.1) | 87 (37.3) |
|  Current, n (%) | 308 (27.2) | 18 (6.7) | 24 (28.6) | 29 (12.0) | 150 (48.7) | 87 (37.3) |
| Alcohol use, n (%) | 556 (49.0)\*\* | 117 (43.8) | 31 (36.9) | 95 (39.3) | 209 (67.9) | 104 (44.6) |
| Systolic blood pressure (mmHg) | 124.0 ±14.0\*\* | 122.0 ±11.2 | 125.3 ±15.0 | 127.3 ±12.5 | 125.3 ±16.0 | 120.6 ±14.0 |
| Medications for hypertension, n (%) | 111 (9.8)\*\* | 19 (7.1) | 14 (16.7) | 48 (19.8) | 17 (5.5) | 13 (5.6) |
| Hypertension, n (%) | 254 (22.4)\*\* | 35 (13.1) | 26 (31.0) | 77 (31.8) | 83 (27.0) | 33 (14.2) |
| Glucose | 105.1 ± 18.1\*\* | 101.0 ± 13.5 | 101.8 ± 16.1 | 111.0 ± 20.7 | 107.0 ± 18.8 | 102.6 ± 17.9 |
| Medications for diabetes, n (%) | 21 (1.9)\*\* | 2 (0.8) | 1 (1.2) | 11 (4.6) | 6 (2.0) | 1 (0.4) |
| Diabetes, n (%) | 80 (7.1)\* | 9 (3.4) | 7 (8.3) | 26 (10.7) | 19 (6.2) | 19 (8.2) |
| LDL-C (mg/dl) | 127.1 ± 34.9\* | 135.0 ± 33.7 | 129.4 ± 40.6 | 121.1 ± 33.0 | 132.5 ± 35.6 | 116.5 ± 31.4 |
| HDL-C (mg/dl) | 50.2 ± 13.5\*\* | 48.1 ± 13.0 | 52.1 ± 17.3 | 51.2 ± 12.2 | 54.1 ± 13.6 | 45.7 ± 11.9 |
| Total cholesterol (mg/dl) | 207.9 ± 37.9\* | 211.9 ± 37.6 | 208.2 ± 45.6 | 206.6 ± 36.9 | 217.4 ± 36.1 | 192.3 ± 33.6 |
| Triglyceride (mg/dl) | 131.5\*\*(85, 190) | 128.0(90.0, 185.0) | 108.0(77.5, 169.0) | 141.5(92.0, 224.0) | 136.5(103.5, 182.0) | 129.0(96.0, 196.0) |
| Medications for hyperlipidemia, n (%) | 105 (9.3)\*\* | 32 (12.0) | 7 (8.3) | 52 (21.5) | 11 (3.6) | 3 (1.3) |
| Hyperlipidemia, n (%) | 781 (68.9) | 195 (73.0) | 52 (61.9) | 172 (71.1) | 208 (67.5) | 154 (66.1) |
| CAC score | 0 (0, 4.5)\*\* | 0 (0, 10.7) | 0 (0, 7.7) | 0 (0, 22.9) | 0 (0, 1.5) | 0 (0, 1.4) |
| CAC score>10, n (%) | 215 (19.0)\*\* | 68 (25.5) | 19 (22.6) | 71 (29.3) | 36 (11.7) | 21 (9.0) |
| Mean HU value from T12-L3 | 175.4 ± 36.3\*\* | 170.8 ± 32.8 | 211.4 ± 39.6 | 177.4 ± 37.7 | 164.5 ± 34.0 | 180.0 ± 31.1 |

The mean ± standard deviation is shown unless otherwise mentioned. The median (interquartile range) is shown in triglyceride and the CAC score. BMI = body-mass index; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; CAC = coronary artery calciﬁcation

The differences of each variable among races were calculated using Chi-squared test for binary or categorical variables, ANOVA for continuous variables with normal distributions, Kruskal-Willis rank test for continuous variables with skewed distributions. \* p-value<0.05, \*\* p-value<0.01

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