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Original Article

Predicting Coronary Artery Calcification by Using the Difference in Bone Mineral Densities of the Spine and Hip: A Retrospective Cross-Sectional Study in Korea

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ABSTRACT

Background/Purpose: The T-score of the lumbar spine rather than that of the hip can be affected by coronary artery calcification because of the anatomic location of these structures. Thus, the discordance in the T-score between the lumbar spine and hip, as assessed using dual-energy X-ray absorptiometry (DXA), may reflect the coronary artery calcium score (CACS). This study aimed to develop a new method for predicting coronary artery calcification based on discordance of the T-score between the lumbar spine and hip.

Methods: This study enrolled 468 asymptomatic participants without a history of cardiovascular disease and osteoporosis between March 2012 and March 2017. Participants were screened using multi-detector computed tomography to determine CACS, and bone health was assessed using DXA.

Results: The differences in T-scores of the lumbar spine and femoral neck were 0.14±0.92, 0.51±1.11, and 0.55±0.93 in the CACS groups <100, 100–399, and ≥400, respectively; the difference in the T-score was statistically significant according to the CACS group (P=0.006). Differences in T-scores between the lumbar spine and femoral neck were significantly associated with CACS (r=0.113, P=0.014). After adjusting for age, sex, body mass index, smoking status, current treatment for hypertension or dyslipidemia, uric acid, and C-reactive protein, the adjusted odds ratio of CACS >100 for the difference in the T-score was 1.36 (95% CI: 1.02–1.80, P=0.046).

Conclusion: Clinicians can use information about T-score discordance between the lumbar and femoral neck region to select participants who need further assessment of the coronary arteries.

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1. INTRODUCTION

Bone mineral density (BMD) is measured in the lumbar spine and hip by using dual-energy X-ray absorptiometry (DXA) to check bone health. DXA is routinely recommended for checking bone health in women aged >65 and <65 years with risk factors of osteoporosis and in men aged >70 years.[1,2] Widely recommended DXA is a relatively inexpensive and safe test; although DXA uses ionizing radiation, radiation exposure is very low (0.0009–0.013 mSv).[3] Interestingly, the bone health status of two body parts are often very different. This phenomenon is called T-score discordance and defined as the presence of a difference in the T-scores of an individual patient between two skeletal sites.[4] Various studies have been conducted to determine the cause of discordance of two sites measured by densitometry. The main mechanisms of discordance are adaptive reaction to mechanical strain and difference in the rate of bone loss according to the content of cortical and trabecular bone, which varies by the anatomical site.[5] Furthermore, degenerative sclerosis of the spine including osteophytes and aortic calcification were identified as important factors in increasing the T-score of the lumbar spine.[6,7] This may be because of the location of the coronary artery, which is anatomically near the lumbar spine; thus, the lumbar T-score is affected by degenerative calcification of the coronary artery. Compared with the lumbar spine, the proximal femur is less affected by these calcifications and degenerative changes.

The presence of coronary artery calcium is a marker of vascular injury related to the extent of atherosclerosis.[8] The association between the presence of coronary calcification and the risk of cardiovascular events has been subsequently demonstrated.[9,10] Especially in the asymptomatic elderly population, the coronary artery calcium score (CACS) is an independent predictor of the long-term risk for coronary heart disease.[11] The measurement of CACS is reasonable for cardiovascular risk assessment in asymptomatic adults at an intermediate Framingham risk and in patients at a low-to-intermediate risk.[12] However, the measurement of CACS for screening of coronary artery disease is not recommended for patients at a low or high risk. Nevertheless, because of ethnic differences, the extent and amount of coronary atherosclerosis and coronary artery disease prevalence have a magnitude of differences; therefore, accepting the recommendations of the guidelines as they are is difficult.[13] According to a previous study of asymptomatic healthy Korean population, CACSs were relatively high in younger individuals. The prevalence of CACS >100 was 5.5% of individuals in their 40s, 12.1% of those in their 50s, 30.4% of those in their 60s, and 45.5% of those in their 70s.[14] Hence, detecting patients who need a precise assessment of coronary atherosclerosis is difficult, especially in asymptomatic Asians.

This study aimed to determine the association between CACS and the difference of bone health between two bones (i.e., the lumbar spine and proximal femur), as assessed using DXA, which is recommended as a regular evaluation for bone health. By using DXA data, clinicians may be able to predict which patients will have a high CACS and more carefully select the participants who need their coronary arteries assessed.

2. METHODS

2.1. Ethical Statements

This study was approved by the independent Institutional Review Board of Jeju National University Hospital, Jeju, Korea (approval number: 2016-06-020).

2.2. Participants

In this retrospective, observational study, we reviewed the medical records of men and women aged >50 years who underwent health screening, which included self-reported questionnaires, physical measurements, DXA scanning, and coronary computed tomography angiography (CCTA) in Jeju National University Hospital between March 2012 and March 2017. Exclusion criteria for this study were patients who received treatment for osteoporosis and patients with a known history of cardiovascular disease (myocardial infarction, angina, or stroke). Based on these criteria, 314 men and 154 women were enrolled in this study.

2.3. Calculation of the Coronary Artery Calcium Score

In participants with a heart rate of <60 beats per minute, CCTA was performed using a 64-slice multi-detector computed tomography (CT) scanner (Somatom Definition Edge; Siemens, Erlangen, Germany). The detector configuration was as follows: 64 overlapping slices of 0.6-mm thickness and a dynamic z-focal spot; gantry rotation time, 0.33 seconds; tube voltage, 120 kVp; and 320 mAs. Aortic calcium lesions were considered to be present when three contiguous pixels of >130 Hounsfield units were detected overlying the vessel of interest.[15] CACS was calculated as described by Agatston and determined by summing individual lesion scores from each of the four major coronary arteries (the left main coronary artery, left anterior descending artery, left circumflex artery, and right coronary artery).[16]

2.4. Bone Mass Measurement

BMD (g/cm^2) of the lumbar spine (L1–L4) and proximal femur were measured using standardized protocols by DXA scanning (Discovery W fan-beam densitometer, Hologic Inc., Waltham, MA, USA). In this study, we used an Asian equation to calculate the T-score: (BMD – reference BMD) divided by (reference standard deviation). However, this time, we used Japanese BMD reference values to calculate the T-score, owing to the uncertainty of the bone density data representative of Koreans.

2.5. Statistical Analysis

We compared patients' baseline characteristics according to CACS in the raw sample via one-way analysis of variance tests and the chi-square test, as appropriate. The continuous variables are presented as a mean±standard deviation, and categorical variables are presented as numbers (%). To examine the association between CACS and various variables, Pearson's correlation analysis was performed. Multivariate logistic regression analyses were also performed to assess the relationship between the level of CACS, which is known to increase along with cardiovascular disease, and differences in the bone mass measurement of the lumbar spine and proximal femur. A *P*-value <0.05 was considered statistically significant. For data management and analysis, SPSS version 20.0 (IBM Corp., Armonk, NY, USA) and STATA version 13.0 (StataCorp., College Station, TX, USA) were used.

Table 1. Baseline characteristics of subjects categorized by the coronary artery calcium score.

Variables	CACS			*P* Value
	<100 (n=377)	100-399 (n=64)	≥400 (n=27)	
Age (y)	57.36±5.38	61.81±4.98	60.44±4.89	<0.001
Male sex	236 (62.6)	55 (85.9)	23 (85.2)	<0.001
Height (cm)	16.286±8.32	166.03±6.44	165.53±8.12	0.006
Weight (kg)	67.89±10.53	71.73±9.52	73.51±11.02	0.001
Body mass index (kg/m^2)	25.50±2.75	25.95±2.58	26.72±2.69	0.048
Systolic blood pressure (mmHg)	127.32±13.83	131.76±12.39	135.15±14.31	0.002
Diastolic blood pressure (mmHg)	80.11±9.75	81.06±7.77	79.96±9.64	0.756
C-reactive protein (mg/L)	0.18±0.37	0.13±0.16	0.26±0.43	0.230
Uric acid (mg/dL)	5.58±1.30	5.95±1.28	6.60±1.57	<0.001
Total cholesterol (mg/dL)	210.45±37.09	202.60±39.12	198.50±42.86	0.115
Triglyceride (mg/dL)	126.84±82.25	132.79±76.68	129.92±66.39	0.856
HDL-C (mg/dL)	51.89±12.70	48.65±12.30	46.92±9.29	0.034
LDL-C (mg/dL)	132.16±33.58	126.76±35.12	126.08±41.26	0.383
25-OH vitamin D (ng/mL)	24.10±8.37	27.40±8.96	26.47±9.08	0.009
Bone mineral density (g/cm^2)				
Total femur	0.92±0.13	0.96±0.13	0.96±0.15	0.067
Femoral neck	0.77±0.12	0.80±0.12	0.80±0.13	0.188
Lumbar spine	0.97±0.14	1.04±0.17	1.05±0.14	<0.001
T-score				
Total femur	0.16±0.91	0.27±0.87	0.25±1.07	0.583
Femoral neck	-0.48±1.04	-0.32±0.99	-0.28±1.03	0.382
Lumbar spine	-0.34±1.16	0.18±1.40	0.25±1.19	<0.001
ΔT-score (lumbar spine – femoral neck)	0.14±0.92	0.51±1.11	0.55±0.93	0.003
Smoking status, current	168 (56.6)	34 (61.8)	16 (76.2)	0.182
Alcohol intake, ever	184 (70.2)	32 (74.4)	13 (81.2)	0.569
Exercise, three times a week or more	127 (43.6)	38 (71.7)	11 (52.4)	0.001
Hypertension	963 (27.3)	28 (49.1)	16 (66.7)	<0.001
Dyslipidemia	61 (18.2)	14 (25.0)	7 (30.4)	0.210

Values are presented as a mean±standard deviation or number of subjects (%). CACS, coronary artery calcium score; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

3. RESULTS

3.1. General Characteristics of the Participants

Of 468 individuals with fully evaluable CCTA and DXA, 377 (80.5%) had CACS <100, 64 (13.6%) had CACS 100–399, and 27 (5.8%) had CACS >400. As listed in Table 1, the average age was the highest in the CACS 100-399 group. CACS was strongly associated with body mass index (BMI), systolic blood pressure, current treatment for hypertension, the uric acid level, high-density lipoprotein cholesterol level, 25-OH vitamin D, and exercise pattern. However, no association was found between CACS and diastolic blood pressure, levels of C-reactive protein and low-density lipoprotein cholesterol, treatment of dyslipidemia, smoking status, and habitual alcohol drinking. Both BMD and T-scores of the lumbar spine were higher in the CACS >400 group than in the CACS <100 and CACS 100–399 groups (all *P* <0.001). However, no significant difference was observed in the BMD and T-scores of the femur in all groups. The different T-scores between the lumbar spine and femoral neck showed a significant positive relationship according to the CACS groups (*P*=0.003).

3.2. Association Between the Coronary Artery Calcium Score and Difference in Bone Health of the Lumbar Spine and Femur

Table 2 demonstrates the potential variables that can affect CACS. Age, male sex, diastolic blood pressure, uric acid level, smoking status, and treatment of dyslipidemia were significantly correlated with CACS. Like the above variables, differences in the T-scores difference of the lumbar spine and femoral neck were significantly associated with CACS (r=0.113, P=0.014).

To determine the difference in the association between bone health and CACS, multivariate logistic regression was performed. Table 3 displays the adjusted odds ratio of CACS >100, which was the point of CACS that was >19.4% in all participants, and the differences in bone health of the lumbar and femoral neck. Across the models, patterns of independent associations were similar regarding the difference in the T-score. According to the results of the final model, which was adjusted for age, sex, BMI, smoking status, current treatment for hypertension or dyslipidemia, and levels of uric acid or C-reactive protein, the odds ratio of the difference in the T-score was 1.36 (95% confidence interval: 1.02–1.80).

4. DISCUSSION

Coronary calcification is proportional to the total amount of atherosclerotic plaques in the coronary arteries, and it is an indicator of coronary artery stenosis. It is also an independent risk factor for ischemic heart disease.[9,17] Unfortunately, although several studies are available, the indications for cardiac CT in predicting future heart diseases are controversial.[12,18] In this cross-sectional study, we presented a new way to screen out participants who are expected to have an increased magnitude of cardiac calcification burden via DXA, which is a noninvasive, convenient, inexpensive, and widely used technique. We found a correlation between CACS and the difference between bone health values checked using DXA in the lumbar spine and proximal femur. This correlation was maintained after adjusting for co-factors that could affect coronary artery calcification. This study suggests that the difference in bone health between the lumbar spine and femur assessed using DXA is an independent indicator of an increased risk for coronary artery calcification.

The association between aortic calcification and discordance of the T-score between two sites measured by densitometry in our study is similar in previous studies. According to a previous study of healthy postmenopausal women, women with calcification showed less loss of BMD than participants without calcification, even though the rates of loss of BMD were similar.[19] Previous studies have mainly evaluated calcification by relying on x-rays. However, one study evaluated the calcium by CT in 20 osteoporotic women, and in that report, the effect of aortic calcification as an artifact was 4%.[20] Another study demonstrated that with an increase from lumbar vertebra 1 to 4, the average aortic calcification increased by up to 2 mm.[5]

There is a point to consider in the evaluation of coronary artery stenosis with CACS, which is an overall

Table 2. Correlation between the coronary artery calcium score and other variables.

Variables	Pearson's Coefficient	*P* Value
Age	0.184	<0.001
Male sex	0.140	0.002
Body mass index	0.088	0.056
Systolic blood pressure	0.147	0.002
Diastolic blood pressure	-0.003	0.950
C-reactive protein	0.034	0.469
Uric acid	0.138	0.003
Total cholesterol	-0.067	0.151
Triglyceride	0.008	0.863
HDL-C	-0.071	0.126
LDL-C	-0.047	0.315
Smoking status, current	0.178	0.001
Alcohol intake, ever	0.080	0.154
Exercise, three times a week or more	0.041	0.439
Hypertension	0.081	0.408
Dyslipidemia	0.125	0.010
ΔT-score (lumbar spine – femoral neck)	0.113	0.014

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 3. Adjusted OR of the coronary artery calcium score >100 in the difference between T-scores of the lumbar spine and femoral neck.

	CACS <100	CACS ≥100	*P* Value
ΔT-score Model 1	1	1.44 (1.10-1.87)	0.007
Model 2	1	1.34 (1.01-1.78)	0.042
Model 3	1	1.36 (1.02-1.80)	0.046

Values are expressed as an odds ratio (95% confidence interval). CACS, coronary artery calcium score; OR, odds ratio.
Model 1: adjusted for age, sex, and body mass index.
Model 2: adjusted for age, sex, body mass index, smoking status, and current treatment for hypertension or dyslipidemia.
Model 3: adjusted for age, sex, body mass index, smoking status, current treatment for hypertension or dyslipidemia, uric acid, and C-reactive protein.

indirect evaluation method. CACS is highly sensitive to the absence of coronary artery stenosis (<50%), but it shows only moderate specificity for the presence of ≥50% of angiographic stenosis.[21] CACS provides additional predictive power for coronary artery disease in asymptomatic patients, but there is direct evidence that this selection reduces coronary artery disease morbidity; moreover, mortality remains unclear. These phenomena may be because most acute coronary events are due to rupture or a vulnerable or unstable plaque and not fixed, high-grade stenosis. However, CACS may not directly identify plaques that are prone to rupture.[22] Nevertheless, patients with extensive coronary artery calcification are likely to have a large burden of non-calcified plaques.[23] Thus, patients with high CACS have a high likelihood of having plaques that are prone to rupture. It is also important to consider that the prognosis of coronary artery stenosis not <50% is not equal to that of the normal coronary artery and that more proximal coronary artery lesions equate to a worse prognosis.[24] Because of vascular remodeling, there is a compensatory enlargement of arteries in early atherosclerosis that serves to accommodate the growing plaque.[25] As a result, extensive coronary artery calcification may be present before the plaque burden overwhelms vascular remodeling and begins to encroach upon the vessel lumen, leading to clinically relevant stenosis.

We need to address the methodological limitations of this study. First, the subjects of this study were relatively healthy adults, who voluntarily participated in health screenings at a hospital. Therefore, it is difficult to represent the entire population with these data. Thus, there may be selection bias. The second issue is related to calcium intake. We could not check the amount of calcium intake by food or supplementation. However, calcium intake by food in Koreans is less than the daily requirement, and most subjects took calcium supplements irregularly.[26] Moreover, calcium consumption was not closely linked to vascular calcification.[27] The third issue is the anatomic features, such as the number of vessels involved and the presence of proximal coronary artery disease, that add to the Agatston score for predicting major coronary heart disease events.[28] These measures may enable refinement of models using CACS to stratify patients for risk reduction management. The fourth issue is that we could not consider the factors that elevated the lumbar T-score, such as osteophytes, undiagnosed minor compression fractures, and hyperparathyroidism. However, our study participants were relatively young to have bony sclerosis or compression fracture, and we already excluded participants taking osteoporosis medication. However, in future studies, these limitations must be considered.[29,30]

5. CONCLUSION

The difference of T-score between the lumbar spine and femur with regard to bone health assessed using DXA is correlated with CACS. In participants who have a significant bone health difference between the lumbar spine and femur, clinicians may consider whether it is necessary to evaluate the status of the coronary artery.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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Ethical Standards: This study was approved by the independent Institutional Review Board of Jeju National University Hospital, Jeju, Korea (approval number: 2016-06-020).

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