

# The association between low bone mineral density and coronary artery calcification in osteoporotic and non-osteoporotic patients in a tertiary center in Saudi Arabia

Ahmed L. Fathala,<sup>a</sup> Sami Alkulaibi,<sup>a</sup> Abdulrahman Khawaji,<sup>a</sup> Abdelghafour Alomari,<sup>b</sup> Ahmed Almuhaideb<sup>a</sup>

From the <sup>a</sup>Department of Radiology, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia; <sup>b</sup>Department of Family Medicine, Department of Radiology, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

**Correspondence:** Dr. Ahmed L. Fathala · MBC 28, Department of Radiology, King Faisal Specialist Hospital and Research Centre, PO Box 3354, Riyadh 11211, Saudi Arabia · ahm35799@hotmail.com · ORCID: <https://orcid.org/0000-0002-2436-4226>

**Citation:** Fathala AL, Alkulaibi S, Khawaji A, Alomari A, Almuhaideb A. The association between low bone mineral density and coronary artery calcification in osteoporotic and non-osteoporotic patients in a tertiary center in Saudi Arabia. *Ann Saudi Med* 2021; 41(2): 101-108. DOI: 10.5144/0256-4947.2021.101

**Received:** December 28, 2020

**Accepted:** February 6, 2021

**Published:** April 1, 2021

**Copyright:** Copyright © 2021, *Annals of Saudi Medicine*, Saudi Arabia. This is an open access article under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC BY-NC-ND). The details of which can be accessed at <http://creativecommons.org/licenses/by-nc-nd/4.0/>

**Funding:** None.

**BACKGROUND:** Cardiovascular disease (CVD) and osteoporosis are major health-care concerns worldwide. The evidence is contradictory on whether a relationship exists between low bone mineral density (BMD) determined by dual-energy absorptiometry (DXA scan) and coronary artery calcification (CAC) measured by computed tomography. Currently, there are no data on patients from Saudi Arabia.

**OBJECTIVE:** Examine the relationship between CAC and BMD in both genders and study the influence of traditional coronary artery disease (CAD) risk factors and osteoporosis.

**DESIGN:** Retrospective, cross-sectional, analytical.

**SETTING:** Single tertiary care center.

**PATIENTS AND METHODS:** We searched radiology databases for patients who underwent both DXA and CAC score scanning within six months of each other. The inclusion criterion was an absence of any history of CAD.

**MAIN OUTCOME MEASURE:** Association between osteoporosis and CAC.

**SAMPLE SIZE:** 195 (34 osteoporotic, 161 normal BMD or osteopenic)

**RESULTS:** Most of the study population (57.4%) were females. The mean age of all patients was 63.6 (10.1) years. Participants with CAC scores of 0 were significantly younger than those who had CAC scores >0. The presence of diabetes mellitus, hypertension, and hypercholesterolemia was higher in patients with CAC scores >0. CAC score and other CAD risk factors were not significantly different between the osteoporotic and nonosteoporotic groups, except for body mass index. A high CAC score (>100) was present in 28%, 20%, 11%, and 30% of participants with no osteoporosis, osteoporosis of the lumbar spine, osteoporosis of the femoral neck, and participants with osteoporosis of both the lumbar spine and femoral neck, respectively ( $P=.762$ ), suggesting there is no association between CAC and the presence of osteoporosis.

**CONCLUSIONS:** Osteoporosis is not associated with higher CAC scores in Saudi Arabia and CAD risk factors are not significantly prevalent in osteoporosis. It appears that CAC and osteoporosis are independent age-related diseases that share common risk factors.

**LIMITATIONS:** Single-center, retrospective.

**CONFLICT OF INTEREST:** None.

Cardiovascular disease (CVD) and osteoporosis are two major healthcare concerns with increasing prevalence worldwide.<sup>1</sup> The two conditions share similar risk factors, such as age, physical inactivity, smoking, increased age, post-menopausal status in women, vitamin D deficiency, and an unhealthy diet.<sup>2,3</sup> Prior studies have reported a relationship between osteoporosis and CVD, stroke, peripheral arterial disease, as well as cardiovascular mortality.<sup>4,5</sup> A recent review article reported that low bone mineral density (BMD) has a significant association with CVD in men aged 50 years and over and postmenopausal women.<sup>6</sup> However, there are still controversies as to whether the relationship between osteoporosis and CVD is independent of age, ethnicity, gender, and conventional CVD risk factors.<sup>2,7</sup>

Coronary artery calcification (CAC) is a well-established marker for overall atherosclerotic plaque burden. A high CAC score has been associated with the presence of obstructive coronary artery disease (CAD) and cardiovascular mortality.<sup>8,9</sup> There is an inconsistent relationship between low bone mineral density (BMD) determined by dual-energy absorptiometry (DXA) and CAC measured by computed tomography (CT). Some studies have found no association between BMD or volumetric BMD and the presence of CAC or aortic calcification,<sup>10,11</sup> while other studies have demonstrated a positive relationship between the presence of aortic calcification and CAC and BMD.<sup>12-16</sup> This positive correlation may be related to age, shared risk factors such as smoking, and other possible contributing factors such as hormones or inflammatory cytokines.<sup>17</sup> The inconsistent findings on any relationship between BMD and CAC may be due to sex- and/or ethnicity-specific differences. Furthermore, longitudinal studies investigating the association between BMD and CAC have been performed mainly in patients with chronic kidney disease, and the results have been inconsistent.<sup>18,19</sup>

CVD is a major concern in the Gulf Cooperation Council countries, including Saudi Arabia, where it is estimated that CVD accounts of more than 45% of all deaths.<sup>20</sup> Also, epidemiological data shows that 34.0% of Saudi women and 30.7% of men between 50 and 79 years of age are osteoporotic, and the prevalence of osteoporosis is expected to increase with increased life expectancy.<sup>20</sup> The high prevalence of osteoporosis in Saudi Arabia may be due to several factors, including lack of physical activity, low calcium intake, a higher prevalence of vitamin D deficiency, and lifestyle factors.<sup>21</sup> The racial differences in BMD and CAC are well known. Only a few studies have reported an association between BMD and CAC in a multiethnic group in one country and there are no international studies.<sup>21,22</sup>

Currently, no study has assessed the relationship between CAC and BMD among both genders in Saudi Arabia. This study was designed to investigate the relationship between CAC and the level of BMD in both genders in Saudi Arabia and analyze the influence of age, gender, and other traditional CAD risk factors on CVD and osteoporosis.

## PATIENTS AND METHODS

The study population consisted of patients who underwent both BMD for osteoporosis screening and CAC score scanning for CAD risk stratification within six months of each other between January 2018 to February 2020. Participants with prior known CAD—such as patients with prior coronary artery bypass surgery, prior percutaneous coronary intervention, or an abnormal stress test—were excluded from the study. Also, patients with a known metabolic bone disease or diagnosed osteoporosis were excluded. All investigations were carried out in accordance with the Declaration of Helsinki. The study methods were approved by the institutional review board (hospital ethics approval #2191294 dated 11 November 2019).

The calcium score was obtained by multislice CT.<sup>23</sup> Electrocardiographic triggered image acquisition was performed with a thickness of 3 mm from the level of the carina to the level of the diaphragm at mid-diastole phase at 60%-80% of the R-R interval. The scan was reviewed and reported by an experienced cardiovascular radiologist who was blinded to participant characteristics or the results of the DXA scan. The CAC analysis was based on the presence or absence of CAC, and the severity of CAC was divided further into two groups as mild (from CAC score 0 to 100) or severe CAC (CAC score >100).

The BMD of both the lumbar spine (L1-L4) and femoral neck was measured using Lunar Prodigy PA +300164 DXA. Daily quality assessments were performed on the DXA machine to ensure the scanner's reliability. BMD results were reported as T-scores, and the scores were categorized as normal/osteopenic (T-score  $\leq$ -1 and -2.5) or osteoporitic BMD (T-score <-2.5).

Analysis of the data was conducted using R software version 3.6.3., *blorr* package. Categorical data are represented as count (%). Chi-square or Fisher's exact test was done to examine the relationship between two qualitative variables. Continuous data were presented as mean and standard deviation (SD), while a *t* test was used to compare continuous variables. Multiple logistic regression was used to assess the relationship between risk factors and CAC, with CAC as the dependent variable ( $\leq$  100 or >100 coronary artery calcium score). The logistic regression model was derived from a full model with all

variables by backwards stepwise reduction. For all tests, a *P* value <.05 was considered statistically significant.

## RESULTS

Of 195 participants, 83 (42.6%) were males. The mean age of the participants was 64 (10) years. The mean age of patients with a CAC score of 0 was significantly lower than those who had CAC score >0 (Table 1). Moreover, 33 (30%) of the CAC >0 patients had a family history of CAD while only 12 (14%) CAC 0 patients had family history of CAD. The percentage of participants who suffer from diabetes mellitus, hypertension, and hypercholesterolemia in the group with CAC >0 was nearly twice the number of participants in the group with a CAC 0 score, and these differences were statistically significant. There were no significant differences in gender, smoking status, steroid, and T-score among CAC groups. Thirty-four patients had a T-score  $\leq$ -2.5 (osteoporotic) while 161 had a T-score  $>$ -2.5 (normal or osteopenic).

None of the CAD risk factors were significantly different between osteoporotic and nonosteoporotic patients except for body mass index (BMI) and hypercholesterolemia (Table 2). BMI was higher in nonosteoporotic patients and hypercholesterolemia was more frequent in nonosteoporotic patients. The age of participants with CAC scores >100 was significantly higher than those with lower CAC scores (Table 3). Also, there was a positive association between family history of CAD and a higher CAC score (*P*=.021). There was no significant difference for gender, smoking, or the mean BMI among

the low and high CAC groups. For diabetes mellitus, hypertension, and hypercholesterolemia, the frequency in patients with high CAC scores significantly exceeded those with low CAC scores. For use of steroids, BMD of the lumbar spine and/or femoral neck, and T-scores, there was no significant difference among the CAC groups. In the comparison of risk factors by high and low CAC groups within the genders, males and females only differed for a family history of CAD, which was statistically significant only in females (Table 4).

The multiple logistic regression analysis indicated that CAC is associated with increasing age and male gender (Table 5). Each one year increase in age was associated with a 6% increase in the risk of having a higher CAC score versus a low score. For males, the risk of a high CAC score was more than three times that of females. Hypertension carried a risk of a high CAC score more than four times that of people of normal blood pressure. A high CAC score (>100) was present in 52 (27%) of patients with no osteoporosis, 20% with osteoporosis of the lumbar spine, 11% with osteoporosis of the femoral neck, and 30% with osteoporosis of both the lumbar spine and femoral neck, but the differences were not statistically significant (*P*=.762), which confirms the finding of no association between CAC score and the presence of osteoporosis (Table 6).

## DISCUSSION

To the best of our knowledge, this is the first study in Saudi Arabia and the Middle East designed to investi-

**Table 1.** Demographic and clinical and characteristics of the study population based on presence and absence of coronary artery calcification.

Factors	Total (n=195)	CAC score 0 (n=85)	CAC >0 (n=110)	P value
Age (years)	63.6 (10.0)	59.2 (9.7)	67.0 (9.0)	<.001
Male	83 (42.6)	35 (41.2)	48 (43.6)	.73
Female	112 (57.4)	50 (58.8)	62 (56.4)	
Family History of CAD	45 (23.1)	12 (14.1)	33 (30.0)	.001
Smoking	6 (3.1)	2 (2.4)	4 (3.6)	.698
Body mass index (kg/m <sup>2</sup> )	30.9 (10.4)	30.7 (11.1)	31.0 (9.9)	.821
Diabetes mellitus	93 (47.7)	26 (32.9)	65 (59.1)	<.001
Hypertension	103 (52.8)	37 (43.5)	66 (60.0)	.022
Hypercholesterolemia	61 (31.3)	18 (21.2)	43 (39.1)	.007
Steroid use	7 (3.6)	3 (3.5)	4 (3.6)	.999
T score lumbar spine and/or femoral neck $\leq$ -2.5	34 (17.4)	14 (16.5)	20 (18.2)	.755

Data are n (%) or mean and standard deviation. CAD; coronary artery disease, CAC score; coronary artery calcium score.

gate the relationship between CAC and osteoporosis. In this study, we demonstrated that there is no association between CAC and osteoporosis diagnosed by DXA scans among Saudi men or women. Our results are in line with previous similar studies performed in

different populations and regions in the world that reported no significant association between osteoporosis and CAC. For instance, the Rotterdam study showed no association between CAC and BMD or CAD risk factors, except for BMD loss, which was higher in women with

**Table 2.** Demographic and clinical and characteristics of the study population in normal and osteoporotic patients.

Factors	Total (n=195)	T score >-2.5 (n=161)	T score lumbar spine and femoral neck ≤-2.5 (n=34)	P value
Age (years)	63.6 (10.1)	63.93 (9.7)	62.2 (11.6)	.408
Male	83 (42.6)	64 (39.8)	19 (55.9)	.084
Female	112 (57.4)	97 (60.2)	15 (44.1)	
Family history of CAD	45 (23.1)	39 (24.2)	6 (17.6)	.408
Smoking	6 (3.1)	6 (3.7)	-	.593
Body mass index (kg/m <sup>2</sup> )	30.9 (10.4)	31.7 (11.0)	27.1 (5.0)	<.001
Diabetes mellitus	93 (47.7)	76 (47.2)	17 (50.0)	.767
Hypertension	103 (52.8)	90 (55.9)	13 (38.2)	.061
Hypercholesterolemia	61 (31.3)	57 (35.4)	4 (11.8)	.007
Steroid	7 (3.6)	7 (4.3)	0 (0.0)	.608
CAC score	151.8 (347.6)	159.6 (355.9)	115.2 (307.5)	.461

Data are n (%) or mean and standard deviation. CAD; coronary artery disease, CAC score; coronary artery calcium score

**Table 3.** Demographic and clinical and characteristics of the study population based on low (CAC score ≤ 100) and high coronary artery calcification (CAC score >100).

Factors	Total (n=195)	Low CAC (CAC <100) (n=143)	High CAC (CAC >100) (n=52)	P value
Age (years)	63.6 (10.1)	62.0 (9.8)	68.0 (9.6)	<.001
Male	83 (42.6)	57 (39.9)	26 (50.0)	.21
Family history of CAD	45 (23.1)	27 (18.9)	18 (34.6)	.021
Smoking	6 (3.1)	4 (2.8)	2 (3.8)	.71
Body mass index (kg/m <sup>2</sup> )	30.9 (10.4)	30.5 (10.9)	31.9 (8.8)	.36
Diabetes mellitus	93 (47.7)	58 (40.6)	35 (67.3)	<.001
Hypertension	103 (52.8)	63 (44.1)	40 (76.9)	<.001
Hypercholesterolemia	61 (31.3)	36 (25.2)	25 (48.1)	.002
Steroid use	7 (3.6)	7 (4.9)	-	.19
BMD lumbar spine	1.01 (0.187)	1.00 (0.181)	1.03 (0.203)	.38
BMD femoral neck	0.822 (.156)	0.817 (.155)	0.834 (0.158)	.5
T score of FN and or LS <-2.5	34 (17.4)	27 (18.9)	7 (13.5)	.378

Data are n (%) or mean and standard deviation. CAD: coronary artery disease, CAC score: coronary artery calcium score, BMD: bone mineral density, LS: lumbar spine, FN: femoral neck.

high CAC scores during follow up, an association that may be related to low estrogen level.<sup>24</sup> Similarly, a prior study demonstrated that the association between the presence of subclinical coronary calcification and low BMD among middle-aged men and women was not significant after controlling for age and other risk factors for CAD and osteoporosis.<sup>25</sup> Additionally, a cross-sectional study designed to investigate the results between BMD and quantitative computerized tomography and CAC measured by electron beam computerized tomography in 313 postmenopausal women and 167 men found that there was no association between osteoporosis and CAC after controlling for age.<sup>11</sup>

In contrast, several studies have shown an inverse association between BMD and CAC.<sup>26-28</sup> This inverse relationship may be related to age, shared risk factors (smoking), or other common pathophysiological mechanisms for osteoporosis and CAD (hormones of inflammatory cytokines).<sup>2</sup> Furthermore, the inconsistent relationship between CAC and BMD may be due to sex- and/or ethnicity-specific differences.<sup>17</sup> In addition, other possible explanations for the inconsistent relationship between osteoporosis and CAC include significant variability in populations, methods, and the anatomical site chosen to assess the osteoporosis and coronary atherosclerosis among different studies.

As in previous studies that have investigated the prevalence of CAC in asymptomatic patients, our study showed that the prevalence of CAC is 56% in the total study population, which is also consistent with our prior report.<sup>29</sup> In addition, there was a significant positive association between the presence of CAC and age, family history of CAD, diabetes mellitus, hypertension, and dyslipidemia ( $P$  value  $<.05$ ). However, there was no positive association between the T-score of the lumbar spine or the T-score of the femoral neck, which suggests that low bone density and CAC are independent of major cardiovascular risk factors such as diabetes mellitus, dyslipidaemias, and hypertension or whether sex-specific differences exist. However, some studies have demonstrated that atherosclerosis and osteoporosis share common risk factors such as aging, dyslipidemia, oxidative stress, diabetes, hypertension, and inflammation.<sup>30,31</sup> Also, our data did not reveal a positive association between absolute CAC score (CAC score  $<100$  and CAC score  $>100$ ) and other CAD risk factors in osteoporotic and nonosteoporotic participants except for BMI, which was higher in nonosteoporotic patients. Surprisingly, in our patient population, the CAC score was higher in nonosteoporotic patients (159 vs. 115), but there was no statistically significant difference between the two groups. Therefore, our study shows no

**Table 4.** Coronary artery disease risk factors in patients by low ( $\leq 100$ ) or high ( $>100$ ) coronary artery calcium score by gender.

	Female			Male		
	Low (CAC $\leq 100$ ) (n=86)	High (CAC $>100$ ) (n=26)	P value	Low (CAC $\leq 100$ ) (n=57)	High (CAC $>100$ ) (n=26)	P value
Age, years	64.6 (7.9)	70.7 (9.2)	.004	58.2 (11.1)	65.3 (9.4)	.004
Family History of CAD	15 (17.4)	10 (38.5)	.024	12 (21.1)	8 (30.8)	.337
Smoking	0 (0)	1 (3.8)	.232	4 (7.0)	1 (3.8)	.999
Body mass index (kg/m <sup>2</sup> )	30.8 (7.9)	33.0 (7.1)	.180	30.0 (14.4)	30.8 (10.2)	.792
Diabetes mellitus	39 (45.3)	18 (69.2)	.032	19 (33.3)	17 (65.4)	.006
Hypertension	46 (53.5)	23 (88.5)	.001	17 (29.8)	17 (65.4)	.002
Hypercholesterolemia	27 (31.4)	15 (57.7)	.015	9 (15.8)	10 (38.5)	.023
Steroid use	7 (8.1)	0 (.0)	.198	0 (0.0)	0 (.0)	---
BMD lumbar spine	1.01 (.2)	1.02 (.2)	.88	0.99 (.2)	1.04 (.2)	.29
BMD femoral neck	.82 (.1)	.83 (.1)	.636	.82 (.2)	.84 (.19)	.631
T score of LS and or FN $<-2.5$	13 (15.1)	2 (7.7)	.471	14 (24.6)	5 (19.2)	.592

Data are n (%) except for age (mean, standard deviation). Statistical comparisons are high vs low CAC. CAD: coronary artery disease, CAC score: coronary artery calcium score, BMD: bone mineral density, LS: lumbar spine, FN: femoral neck

significant association between CAC and osteoporosis in men or women with a wide range of CAC scores. Reasons for these results may be that the prevalence of osteoporosis in our population was low compared to other studies. Also, DXA might not be sensitive enough to detect osteoporosis of the lumbar spine in the presence of severe degenerative changes and osteophytes, or the presence of calcific plaques in adjacent vessels.<sup>32,33</sup> Also, it has been reported that volumetric BMD measured by quantitative CT, but not BMD measured by DXA, provides a specific measurement of metabolically active trabecular bone. In one study, volumetric BMD demonstrated a significant association with CAC and vascular calcification at multiple vascular sites but was not measured by DXA.<sup>34</sup>

We found a 17% prevalence of osteoporosis (T-score <-2.5 in either the lumbar spine or femoral neck) with nearly equal distribution of abnormal T-scores in the lumbar spine and femoral neck in both men and women. The studies that have assessed the prevalence of osteoporosis in Saudi Arabia are limited and inconsistent. For example, Sadat et al reported that 34% of healthy Saudi women and 30.7% of Saudi men aged 50–79 years are osteoporotic,<sup>35</sup> whereas the International Osteoporosis Foundation estimated the prevalence of osteoporosis among Saudi women aged 50–70 years to be approximately 23%. Generally, the prevalence of low bone mass is higher in the Middle East than in Western countries, which could be due to the high prevalence of vitamin D deficiency in the Middle East and Africa region compared with Western countries.<sup>36</sup> The mortality rates after hip fracture has also been reported to be

two to three times higher in Middle Eastern countries compared to Western countries.<sup>37</sup> Vitamin D deficiency appears to be involved in the pathogenesis of CAD at several steps.<sup>38</sup> For example, vitamin D deficiency promotes cholesterol uptake by macrophages and thus promotes atherosclerosis.<sup>39</sup> Also, vitamin D deficiency has been found to be associated with a decreased level of high-density lipoprotein, which promotes atherosclerosis.<sup>40</sup> However, taking high dose-vitamin D supplements does not prevent cardiovascular disease, according to the result of a recent large clinical trial.<sup>41</sup>

Only a few studies have explored the prevalence of osteoporosis in Saudi Arabia. Our findings showed that the prevalence of osteoporosis in Saudi Arabia is 17.4% based on a T-score of less than -2.5 in either the lumbar spine or femoral neck or both, with no significant difference between men and women (mean age 62 [12] years). This is in contrast to a prior report that reported the prevalence of osteoporosis as 34% in healthy women and 30.7% in men aged 50–70 years.<sup>35</sup> However, the prevalence of osteoporosis in Saudi women aged 50–70 years was estimated to be approximately 23% based on the International Osteoporosis Foundation. It has also been reported that the prevalence of low bone mass is higher in the Middle East than in Western countries.<sup>42</sup> One of the possible reasons for low BMD in the Middle East is the high prevalence of hypovitaminosis D in the Middle East and African regions compared to Western countries.<sup>36</sup> Also, we observed no significant difference in the traditional CAD risk factors (such as diabetes and smoking) in osteoporotic and nonosteoporotic patients. Higher BMI and dyslipidemia were more common in nonosteoporotic patients. Although both CAD and osteoporosis share similar modifiable risk factors, our data and the available epidemiological evidence do not allow for the establishment of a causal link between CAD and osteoporosis.<sup>43</sup> However, it is clear that both CAD and osteoporosis are a major health burden affecting millions of patients worldwide, and effective treatment strategies can be adapted to address both conditions.

There are several potential limitations to this retrospective study. The number of patients in the study population from a single tertiary referral hospital with

**Table 5.** Multiple logistic regression for variables associated with low ( $\leq 100$ ) or high ( $>100$ ) coronary artery calcium score.

	Odds ratio (95% CI)	P value
<b>Intercept</b>		
Age (years)	1.05 (1.01-1.09)	.0254
Male	3.84 (1.73-9.00)	.0013
Hypertension	4.46 (2.00-10.59)	.0004

Model fit measures: Overall model test:  $P < .001$ , Nagelkerke R<sup>2</sup>: 0.220, Deviance: 194.246

**Table 6.** Distribution of coronary artery calcium score  $>100$  in patients with and without osteoporosis.

	No osteoporosis (n=161)	Osteoporosis of lumbar spine (n=15)	Osteoporosis of femoral neck (n=9)	Osteoporosis of both lumbar spine and femoral (n =10)	P value
CAC score $>100$	45 (28.0)	3 (20.0)	1 (11.1)	3 (30)	.762

Data are n (%). Statistical comparisons by analysis of variance.

a possible high risk for osteoporosis and CAD is small; subsequently, selection bias cannot be excluded. However, the prevalence of CAC in our population was comparable to our prior studies. In addition, due to the limited number of participants and the possibility of a type 2 statistical error, our findings should be interpreted with caution. Although DXA is the standard method for osteoporosis screening and follow-up, DXA may not be the ideal technique to distinguish between bone mineral content and extrasosseous calcification, such as osteophytes, in severe degenerative changes of the lumbar spine. Also, the use of multidetector computed tomography for measurement of CAC could not distinguish medial from intimal calcification.

Finally, large-scale prospective studies are needed to evaluate the possible relationship between CAC and osteoporosis and the efficacy of long-term and early simultaneous assessment of both CAC and BMD in the prevention of disease progression and a reduction in disease-related morbidity and mortality.

In conclusion, our main finding is that osteoporosis of the lumbar spine and/or femoral neck is not associated with higher CAC scores. Our findings suggest that osteoporosis and CAC are not related to each other and CAD risk factors are not significantly more prevalent in osteoporosis. Our findings suggest that CAC and osteoporosis are independent age-related diseases that share common risk factors.

## REFERENCES

- Higgins CL, Marvel SA, Morrisett JD. Quantification of calcification in atherosclerotic lesions. *Arteriosclerosis, thrombosis, and vascular biology*. 2005;25(8):1567-76.
- Farhat GN, Cauley JA. The link between osteoporosis and cardiovascular disease. Clinical cases in mineral and bone metabolism : the official journal of the Italian Society of Osteoporosis, Mineral Metabolism, and Skeletal Diseases. 2008;5(1):19-34.
- Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121(4):586-613.
- Nordström A, Eriksson M, Stegmayr B, Gustafson Y, Nordström P. Low bone mineral density is an independent risk factor for stroke and death. *Cerebrovascular diseases (Basel, Switzerland)*. 2010;29(2):130-6.
- Qu X, Huang X, Jin F, Wang H, Hao Y, Tang T, et al. Bone mineral density and all-cause, cardiovascular and stroke mortality: a meta-analysis of prospective cohort studies. *International journal of cardiology*. 2013;166(2):385-93.
- Ye C, Xu M, Wang S, Jiang S, Chen X, Zhou X, et al. Decreased Bone Mineral Density Is an Independent Predictor for the Development of Atherosclerosis: A Systematic Review and Meta-Analysis. *PLoS One*. 2016;11(5):e0154740.
- von der Recke P, Hansen MA, Hassager C. The association between low bone mass at the menopause and cardiovascular mortality. *The American journal of medicine*. 1999;106(3):273-8.
- Brown ER, Kronmal RA, Bluemke DA, Guerci AD, Carr JJ, Goldin J, et al. Coronary calcium coverage score: determination, correlates, and predictive accuracy in the Multi-Ethnic Study of Atherosclerosis. *Radiology*. 2008;247(3):669-75.
- Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *The New England journal of medicine*. 2008;358(13):1336-45.
- Flipon E, Liabeuf S, Fardellone P, Menvier R, Ryckelynck T, Grados F, et al. Is vascular calcification associated with bone mineral density and osteoporotic fractures in ambulatory, elderly women? *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2012;23(5):1533-9.
- Sinnott B, Syed I, Sevrukov A, Barenholtz E. Coronary calcification and osteoporosis in men and postmenopausal women are independent processes associated with aging. *Calcified tissue international*. 2006;78(4):195-202.
- Hyder JA, Allison MA, Wong N, Papa A, Lang TF, Sirlin C, et al. Association of coronary artery and aortic calcium with lumbar bone density: the MESA Abdominal Aortic Calcium Study. *American journal of epidemiology*. 2009;169(2):186-94.
- Choi SH, An JH, Lim S, Koo BK, Park SE, Chang HJ, et al. Lower bone mineral density is associated with higher coronary calcification and coronary plaque burdens by multidetector row coronary computed tomography in pre- and postmenopausal women. *Clinical endocrinology*. 2009;71(5):644-51.
- Kiel DP, Kauppila LI, Cupples LA, Hannan MT, O'Donnell CJ, Wilson PW. Bone loss and the progression of abdominal aortic calcification over a 25 year period: the Framingham Heart Study. *Calcified tissue international*. 2001;68(5):271-6.
- Hak AE, Pols HA, van Hemert AM, Hofman A, Witteman JC. Progression of aortic calcification is associated with metacarpal bone loss during menopause: a population-based longitudinal study. *Arteriosclerosis, thrombosis, and vascular biology*. 2000;20(8):1926-31.
- Schulz E, Arfai K, Liu X, Sayre J, Gilsanz V. Aortic calcification and the risk of osteoporosis and fractures. *The Journal of clinical endocrinology and metabolism*. 2004;89(9):4246-53.
- Kuipers AL, Zmuda JM, Carr JJ, Terry JG, Patrick AL, Ge Y, et al. Association of volumetric bone mineral density with abdominal aortic calcification in African ancestry men. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2014;25(3):1063-9.
- Barreto DV, Barreto Fde C, Carvalho AB, Cuppari L, Draibe SA, Dalboni MA, et al. Association of changes in bone remodeling and coronary calcification in hemodialysis patients: a prospective study. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. 2008;52(6):1139-50.
- Coen G, Ballanti P, Mantella D, Manni M, Lippi B, Pierantozzi A, et al. Bone turnover, osteopenia and vascular calcifications in hemodialysis patients. A histomorphometric and multislice CT study. *American journal of nephrology*. 2009;29(3):145-52.
- Aljefree N, Ahmed F. Prevalence of Cardiovascular Disease and Associated Risk Factors among Adult Population in the Gulf Region: A Systematic Review. *Advances in Public Health*. 2015;2015:235101.
- Looker AC, Borrud LG, Hughes JP, Fan B, Shepherd JA, Melton LJ, 3rd. Lumbar spine and proximal femur bone mineral density, bone mineral content, and bone area: United States, 2005-2008. *Vital and health statistics Series 11, Data from the National Health Survey*. 2012(251):1-132.
- Bild DE, Detrano R, Peterson D, Guerci A, Liu K, Shahar E, et al. Ethnic differences in coronary calcification: the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation*. 2005;111(10):1313-20.
- Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *Journal of the American College of Cardiology*. 1990;15(4):827-32.
- Campos-Obando N, Kavousi M, Roeters van Lennep JE, Rivadeneira F, Hofman A, Uitterlinden AG, et al. Bone health and coronary artery calcification: The Rotterdam Study. *Atherosclerosis*. 2015;241(1):278-83.
- Lin T, Liu JC, Chang LY, Shen CW. Association between coronary artery calci-

fication using low-dose MDCT coronary angiography and bone mineral density in middle-aged men and women. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2011;22(2):627-34.

**26.** Ahmadi N, Mao SS, Hajsadeghi F, Arnold B, Kiramijyan S, Gao Y, et al. The relation of low levels of bone mineral density with coronary artery calcium and mortality. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2018;29(7):1609-16.

**27.** Wiegandt YL, Sigvardsen PE, Sørgaard MH, Knudsen AD, Rerup SA, Kühl JT, et al. The relationship between volumetric thoracic bone mineral density and coronary calcification in men and women - results from the Copenhagen General Population Study. *Bone*. 2019;121:116-20.

**28.** Barengolts EI, Berman M, Kukreja SC, Kouznetsova T, Lin C, Chomka EV. Osteoporosis and coronary atherosclerosis in asymptomatic postmenopausal women. *Calcified tissue international*. 1998;62(3):209-13.

**29.** Fathala AL, Bukhari SQ, Shoukri M, El Sergani H, Al-Ghamdi B, Al-Sugair A. High prevalence of coronary artery calcification in Saudi patients with normal myocardial perfusion. *Annals of Saudi medicine*. 2017;37(2):154-60.

**30.** Doherty TM, Fitzpatrick LA, Inoue D, Qiao JH, Fishbein MC, Detrano RC, et al.

Molecular, endocrine, and genetic mechanisms of arterial calcification. *Endocrine reviews*. 2004;25(4):629-72.

**31.** Jørgensen L, Joakimsen O, Rosvold Berntsen GK, Heuch I, Jacobsen BK. Low bone mineral density is related to echogenic carotid artery plaques: a population-based study. *American journal of epidemiology*. 2004;160(6):549-56.

**32.** Drinka PJ, DeSmet AA, Bauwens SF, Rogot A. The effect of overlying calcification on lumbar bone densitometry. *Calcified tissue international*. 1992;50(6):507-10.

**33.** Orwoll ES, Oviatt SK, Mann T. The impact of osteophytic and vascular calcifications on vertebral mineral density measurements in men. *The Journal of clinical endocrinology and metabolism*. 1990;70(4):1202-7.

**34.** Carr JJ, Register TC, Hsu FC, Lohman K, Lenchik L, Bowden DW, et al. Calcified atherosclerotic plaque and bone mineral density in type 2 diabetes: the diabetes heart study. *Bone*. 2008;42(1):43-52.

**35.** Sadat-Ali M, Al-Habdan IM, Al-Turki HA, Azam MQ. An epidemiological analysis of the incidence of osteoporosis and osteoporosis-related fractures among the Saudi Arabian population. *Annals of Saudi medicine*. 2012;32(6):637-41.

**36.** Sweileh WM, Al-Jabi SW, Zyoud SH, Sawalha AF, Ghanim MA. Osteoporosis is a neglected health priority in Arab World: a comparative bibliometric analysis. *Springer-Plus*. 2014;3:427.

**37.** Baddoura R, Hoteit M, El-Hajj Fuleihan G. Osteoporotic fractures, DXA, and fracture risk assessment: meeting future challenges

in the Eastern Mediterranean Region. *Journal of clinical densitometry : the official journal of the International Society for Clinical Densitometry*. 2011;14(4):384-94.

**38.** Aggarwal R, Akhthar T, Jain SK. Coronary artery disease and its association with Vitamin D deficiency. *J Midlife Health*. 2016;7(2):56-60.

**39.** Oh J, Weng S, Felton SK, Bhandare S, Riek A, Butler B, et al. 1,25(OH)<sub>2</sub> vitamin D inhibits foam cell formation and suppresses macrophage cholesterol uptake in patients with type 2 diabetes mellitus. *Circulation*. 2009;120(8):687-98.

**40.** Auwerx J, Bouillon R, Kesteloot H. Relation between 25-hydroxyvitamin D<sub>3</sub>, apolipoprotein A-I, and high density lipoprotein cholesterol. *Arteriosclerosis and thrombosis : a journal of vascular biology*. 1992;12(6):671-4.

**41.** Scragg R, Stewart AW, Waayer D, Lawes CMM, Toop L, Sluyter J, et al. Effect of Monthly High-Dose Vitamin D Supplementation on Cardiovascular Disease in the Vitamin D Assessment Study : A Randomized Clinical Trial. *JAMA cardiology*. 2017;2(6):608-16.

**42.** Maalouf G, Gannagé-Yared MH, Ezzedine J, Larijani B, Badawi S, Rached A, et al. Middle East and North Africa consensus on osteoporosis. *Journal of musculoskeletal & neuronal interactions*. 2007;7(2):131-43.

**43.** Warburton DER, Nicol CW, Gatto SN, Bredin SSD. Cardiovascular disease and osteoporosis: balancing risk management. *Vascular health and risk management*. 2007;3(5):673-89.