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# Relationship between Calcium Score and Conventional Risk Factors in the Diagnosis of Atherosclerosis

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## Abstract

**Background:** The coronary artery calcium score has been established as a highly specific feature of coronary atherosclerosis. The present study aimed to assess the possible association of coronary artery risk factors involving atherosclerosis with the coronary artery calcification (CAC) scores using coronary computed tomographic angiography (CCTA).

**Methods:** The present cross-sectional study, performed on 252 patients in need of CCTA during April 2019 and September 2019 at Farshchian hospital in Hamadan, Iran. The demographic information and risk factors were acquired from the files of patients. Furthermore, the CACs of patients were calculated and expressed as the Agatston score. Based on the Agatston scale, participants were divided into 4 CAC scores: zero (CAC = 0), mild (CAC = 1-99), moderate (CAC = 100-399), and severe (CAC ≥400). The association between possible coronary artery disease (CAD) risk variables and the CAC score was investigated using multinomial logistic regression.

**Results:** Of 252 participants, approximately 40% of studied patients had a positive CAC score (CAC > 0). CAC significantly shifts toward higher scores in smokers, patients with diabetes, hypertension, and older patients. Mild (CAC = 1-99) and moderate CAC (100-399) were significantly associated with diabetes (odds ratio [OR], 3.26; 95% CI, 1.48-7.17) and (OR, 12; 95% CI, 4.40-32.71) for mild and moderate CAC, respectively. However, the strongest predictor for severe CAC was diabetes (OR, 7.72; 95% CI, 2.10-28.35).

**Conclusion:** Coronary artery calcium scoring is a marker for risk factors associated with atherosclerosis. In this study, more than half of patients in CAC screening had CAC = 0. The strongest predictor of severe CAC>0 was smoking and diabetes. Regarding this association between health condition and CAC, determining the CAC can prevent major coronary heart disease events in these patients.

**Keywords:** Coronary Artery Calcium Score, Conventional Risk Factors, Atherosclerosis

***Conflicts of Interest:*** *None declared*
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## Introduction

Despite the occurrence of brilliant advances in the field of prevention and treatment, coronary heart disease (CHD) is still known as the most common cause of death throughout the world. Altho ugh it is not possible to precisely recognize the patients at risk of developing coronary artery disease (CAD), influences of certain risk factors, genetic and environmental, have been quite understood (1, 2). The most familiar risk factors include aging, hypertension, diabetes mellitus (DM), smoking, lack of physical activity, mental stress, obesity, and being overweight. On the other hand, coronary artery calcification (CAC) has just been introduced as a noninvasive indicator of CAD (3, 4). The amount of calcium in the coronary arteries can be calculated using cardiac gated computed tomography (CT), and it is usually expressed as a total calcium score. The CAC score, a well-established marker

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***↑What is "already known" in this topic:***
The CAC score is a well-established marker of coronary atherosclerosis.

***→What this article adds:***
According to the results, there was an association between calcium scoring (CACS) and traditional risk factors in atherosclerotic patients.

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of the total burden of coronary atherosclerosis, has significant clinical implications even in the subclinical stages and has also proved to be highly beneficial for risk stratification in asymptomatic patients (5, 6). Besides high sensitivity and moderate specificity of the coronary calcium score in the prediction of significant coronary arterial lesions in angiography, a high correlation with the degree of coronary atherosclerosis in pathologic specimens has also been found (7, 8). Evolving evidence suggests that elevated coronary calcium scores not only predict incident coronary events in asymptomatic populations but also emphasize the strength of risk stratification systems for targeted prevention. However, only limited studies have evaluated the association of the CAC score with traditional coronary risk factors (9-11). Owing to the importance of primary prevention and risk factor modification in the management of CAD, the present article sought the possible relationship between the CAC score and traditional coronary risk factors.

## Methods

### Study Sample

This retrospective analytical cross-sectional study was approved by the ethics committee of Hamadan University of Medical Sciences. Files of 252 patients who underwent coronary computed tomographic angiography (CCTA) in Farshchian subspeciality cardiovascular center in Hamadan from April 2019 to September 2019 were investigated in this research. The patients with a history of coronary artery bypass graft were excluded from the study. Data were collected by gathering the medical records of patients who experienced CCTA during April 2019 and September 2019.

### Risk Factor Acquisition

In this study, the data were collected from files of patients. The demographic information (age, gender), past medical history, current health behaviors, and conventional risk factors of CAD (eg, family history of CAD, DM, hypertension, hyperlipidemia, and smoking) were collected. The body mass index (BMI) (kg/m$^2$) was calculated using self-reported height and weight data. Gender, major health conditions, and other risk factor variables were measured on a nominal scale, whereas age was measured on an interval scale, smoking status was measured on an ordinal scale (current, former, never), and age was recorded on an interval scale (yes, no).

### CAC Score

All CT scans were performed using a 128-slice multidetector CT scanner as per local clinical routine for identifying and assessing CAC. A noncontract-enhanced, prospective, electrocardiogram-gated image acquisition (sequential scan with 128 × 0.6-mm collimation, 100 to 150-mA tube current, tube voltage of 100 kV for BMI <30 and 120 kV for BMI ≥30) was performed to determine the total calcium burden of the coronary tree. Then, contrast-enhanced CT angiography data were acquired with the administration of 70 cc of intravenous nonionic water-soluble contrast media (iodixanol, 320 mg/mL; Visipaque; GE Healthcare) for all patients. Images acquired with retrospective ECG-gated protocol using 128-detector CT scanner (Siemens; SOMATOM Definition AS) with parameters as follow: 128x 0.6 -mm collimation, a 300-millisecond gantry rotation time, 100 to 150-mA tube current, tube voltage of 100 kV for BMI <30, and 120 kV for BMI ≥30. During systole evaluation of coronary arteries, x-ray output was minimized using retrospective electrocardiogram-gated x-ray tube modulation. Datasets were rebuilt in a medium smooth cardiac kernel with a slice thickness of 0.6 mm and increment of 0.3 mm. Data were rebuilt in axial, sagittal, and coronal perspectives.

### CCTA Image Interpretation

We transferred CT data sets to a workstation for image analysis (Aquarius Net Station, Terarecon Inc). The total calcium score was calculated and expressed as an Agatston score. Our patients were divided into 4 groups based on the CCS risk classification definitions of CCS 0, 1-99 (mild), 100-399 (moderate), and > 400 (severe). The CCS >400 was used to designate high-risk CCS. The contrast-enhanced 128-MDCT images with maximum intensity and curved multiplanar reconstruction techniques were reviewed by an independent reviewer, along with various longitudinal axis and transversely. The Agatston score was calculated using noncontract studies. Axial pictures, multiplanar reformations, and maximal intensity projections were used to assess nonobstructive and obstructive CAD using contrast-enhanced imaging. Coronary stenosis was graded using a 17-segment model of coronary arteries and a 4-point grading scale (normal; mild, 50%; moderate, 50% to 69 percent; severe, 70%).

### Statistical Analysis

All statistical analyses were performed using SPSS Version 16.0 software. Statistical significance was defined as $P < .05$. For descriptive analysis, continuous variables were presented as mean ± SD and categorical variables were presented as frequencies with percentages. Statistical analysis of continuous variables was performed using a Student t test and categorical variables using a chi-square test. Pearson correlation coefficients were used to describe the relationship between continuous variables and CACS. The crud odds ratios were provided, together with their 95% CIs.

## Results

### Demographic and Risk Factors

In this cross-sectional study, 252 patients, of whom 52.8% were men and 47.2% were women, met the inclusion criteria and were examined. The most prevalent risk factors in patients were the increase of hypertension (9%), history of cardiovascular disease (1%), lipid disorder (30.2%), and diabetes (17.9%). The median age of patients was 51.97±11.95 years (range, 18-81 years). The average BMI was $27.58 \pm 4.65 kg/m^2$ with a range of 17.03 to 51.87 kg/m$^2$.

### CAC and Prevalence of Risk Factors

Table 1 demonstrates the clinical characteristics for both



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the CAC = 0 and CAC >0 groups. As demonstrated in Table 1, approximately 40% of studied patients had CAC >0. Within the CAC = 0 group, most patients did not have hypertension, diabetes, dyslipidemia, or family history; most of them had a BMI <30 and were younger than 45 years old. The expected distribution of CAC shifts toward higher scores in smokers, patients with diabetes, hypertension, men, and older patients. Among the risk factors, diabetes, smoking, and hypertension showed the highest relationship with a non-zero calcium score. Patients in the CAC >0 groups were older, more likely to be male, and had higher rates of hypertension, diabetes, and dyslipidemia than the patients with a score of CAC = 0. As demonstrated in Table 1, there was no significant difference between the CAC = 0 and CAC > 0 groups for dyslipidemia, family history, and BMI risk factors (P > .05). The results presented in Table 2 show that mild CAC (CAC = 1-99) was significantly associated with hypertension and diabetes. The ORs of CAC based on risk factors count in crud modes. The strongest of mild CAC was diabetes (OR, 3.26; 95% CI, 1.48-7.17). Hypertension also increased the odds of having mild CAC by approximately 3 times (OR, 3.12; 95% CI, 1.71-5.68). Similar to mild CAC, diabetes was the strongest predictor for moderate CAC (100-399). Having diabetes increased the odds approximately 12 times (OR, 12; 95% CI, 4.40-32.71) for moderate CAC. Smoking was the second predictor of moderate CAC (OR, 4.32; 95% CI, 1.52-12.27). Gender was the third strongest predictor for moderate CAC. Being male increased the odds for moderate CAC more than 3 times (OR, 3.88; 95% CI, 1.36-11.02). Severe CAC (CAC > 400) was significantly associated with smoking, diabetes, and family history. Smoking was the strongest predictor for severe CAC with the odds of 7.72 (OR, 7.72; 95% CI, 2.10-28.35). Unlike mild and moderate CAC, smoking significantly increased the odds for severe CAC. However, diabetes was the strongest predictor for mild and moderate CAC and was the second strongest predictor for severe CAC. Compared with nondiabetic patients, having diabetes significantly increased the odds for severe CAC by more than 3 times (OR, 3.75; 95% CI, 0.89-15.76).

## Discussion

Approximately half of all patients with CAD die suddenly or have an acute myocardial infarction, making early detection critical. Early detection of risk factors, clinical and lab data, as well as non-invasive imaging tests in selected patients, allows for the implementation of the best preventative and risk stratification approaches. Several diagnostic approaches for estimating cardiovascular risk and diagnosing subclinical atherosclerosis in asymptomatic patients have been studied in recent decades. Among them, the CAC has demonstrated high accuracy in predicting future events and detecting early diseases that can be isolated or linked to clinical scores (12, 13). The present study was performed to determine the relationship be-

*Table 1.* CAC and Prevalence of risk factors among study participants

| | | CAC Score | | | | | |
|---|---|---|---|---|---|---|---|
| | | Total N (%) | Zero N (%N) | Mild N (%N) | Moderate N (%N) | Severe N (%N) | *P value |
| Overall | | | 154 (61.11) | 65 (25.79) | 22 (8.73) | 11 (4.37) | |
| Risk factors | | | | | | | |
| smoking | Yes | 39 (15.4) | 15 (9.7) | 11(16.9) | 7 (31.8) | 6 (54.6) | 0.001 |
| | No | 213 (84.52) | 139 (90.3) | 54 (83.1) | 15 (68.2) | 5 (45.4) | |
| Diabetes | Yes | 50 (19.8) | 14 (19.1) | 16 (24.6) | 12 (54.5) | 8 (72.7) | |
| | No | 202 (80) | 140 (90.9) | 49 (75.4) | 10 (45.5) | 3 (27.3) | 0.001 |
| Dyslipidemia | Yes | 79 (31.3) | 41 (26.6) | 19 (29.2) | 12 (54.5) | 7 (63.6) | 0.061 |
| | No | 173 (68.6) | 113 (73.4) | 46 (70.8) | 10 (45.5) | 4 (36.4) | |
| Hypertension | Yes | 110 (43.6) | 50 (32.5) | 39 (60) | 12 (54.5) | 9 (81.8) | 0.001 |
| | No | 142 (56.3) | 104 (67.5) | 26 (40) | 10 (45.5) | 2 (18.2) | |
| Family history | Yes | 86 (34.12) | 47 (30.5) | 25 (5/38) | 8 (36.4) | 6 (54.5) | 0.318 |
| | No | 166 (65.87) | 107 (69.5) | 40 (5/61) | 14 (63.6) | 5 (45.5) | |
| Gender | Men | 133 (52.7) | 72 (46.7) | 37 (56.9) | 17 (77.3) | 7 (63.6) | 0.037 |
| | Female | 119 (47.2) | 82 (53.3) | 28 (43.1) | 5 (22.7) | 4 (36.4) | |
| BMI | >=30 | 61 (24.2) | 41 (26.6) | 13 (20) | 6 (27.3) | 1 (9.1) | 0.548 |
| | <30 | 191(75.7) | 113 (73.4) | 52 (80) | 16 (72.7) | 10 (90.9) | |
| Age groups, yr | <45 | 76 (30.1) | 66 (42.9) | 7 (10.8) | - | 3 (27.3) | 0.001 |
| | 46-55 | 75 (29.7) | 49 (31.8) | 24 (36.9) | 1 (4.5) | 1 (9.1) | |
| | >56 | 101 (40) | 39 (25.3) | 34 (52.3) | 21 (95.4) | 7 (63.3) | |

**P*-value< 0.05 is significant.

*Table 2.* Association between non-zero odds ratio and risk factors.

| Risk Factors | CAC score (vs zero(0)) | | |
|---|---|---|---|
| | Mild (1-99) n=65 OR (CI) | Moderate (100-399) n=22 OR (CI) | Severe (>400) n=11 OR (CI) |
| Smoking (vs. never) | 1.88 (0.81-4.36) | 4.32 (1.52-12.27) | 7.72 (2.10-28.35) |
| Diabetes (vs. no) | 3.26 (1.48-7.17) | 12.00 (4.40-32.71) | 3.75 (0.89-15.76) |
| Dyslipidemia (vs no) | 1.13 (0.59-2.16) | 3.30 (1.32-8.23) | 1.57 (0.43-5.66) |
| Hypertension (vs. no) | 3.12 (1.71-5.68) | 2.49 (1.01-6.16) | 0.46 (0.09-2.21) |
| Gender (male vs. female) | 1.50 (0.83-2.70) | 3.88 (1.36-11.02) | 1.99 (0.56-7.08) |
| Family history (vs. no) | 1.42 (0.77-2.60) | 1.30 (0.51-3.31) | 2.73 (0.79-9.36) |
| BMI >30 kg/m (vs. no) | 0.66 (0.26-1.65) | 1.03 (0.37-2.8) | 0.27 (0.03-2.22) |
| Age, yr. | 1.08 (1.05-1.11) | 1.17 (1.10-1.23) | 1.026 (0.99-1.12) |

OR: Odds ratio CI: Confidence interval



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tween the calcium score and common risk factors of atherosclerosis in patients undergoing CT angiography. Many studies showed that CAC is an accurate and powerful tool for assessing the risk of atherosclerosis in asymptomatic patients and is directly related to the known risk factors for atherosclerosis (14, 15). However, our study was performed on symptomatic patients who underwent CCTA. In this study, approximately 40% of the study population had CAC > 0 (25.79% mild CAC; 8.73% moderate CAC; 4, 37% severe CAC). This finding suggests that a significant number of these asymptomatic people have subclinical CAD and would benefit from medical treatment and/or behavioral/lifestyle adjustments. Furthermore, only 4.37% of patients had severe CAC. There was a significant difference between CAC = 0 and CAC > 0 groups in smoking, diabetes, hypertension, and age. In our study, the predictors of severe CAC in terms of risk factors were different from mild to moderate CAC. Diabetes was the strongest predictor for mild to moderate CAC, whereas smoking significantly increased the odds for severe CAC. Smoking significantly increased the odds from 1.88 to 7.72 in mild CAC to severe CAC. Smoking seems to be the strongest predictor for CAC > 100. Diabetes was the strongest predictor in mild and moderate CAC, and the second strongest predictor in severe CAC; this finding could be attributable to the limited sample size of the severe CAC groups. Other health conditions, such as hypertension and dyslipidemia, significantly increased the odds for mild and moderate CAC. Surprisingly, age and BMI were not significant predictors for CAC > 0. In severe CAC, the best predictor was a family history of CAD, which increased the risks by around 3 times (OR, 2.73; 95% CI, 0.79-9.36). Overall, our results were consistent with a previous study that found diabetes (OR, 2.07; 95% CI, 1.47 to 2.90) and smoking (OR, 1.29; 95% CI, 1.02 to 1.63) as the strongest predictor for CAC > 0. According to the results studied by Main et al in 2010, a higher CAC associated with diabetes, smoking, and age over 40, causes CHD in a short time (16). In 2013, Pletcher et al found that CAC was associated with age, sex, race, and all common CAD risk factors, which confirms the findings of our study (17). In 2010, a study by Cademartiri et al also indicated that coronary calcium scores were a good indicator for assessing coronary artery involvement. CHD tends to develop 2 to 4 times more likely in patients with diabetes (18). Vascular diseases are the most important cause of death and disability in patients with diabetes. Diabetes leads to small vessel involvement and its complications, such as nephropathy, neuropathy, and retinopathy, and large vessel involvement (eg, coronary, cerebral, and peripheral arteries). Smoking was also significantly associated with increased odds of CAC > 0, which was consistent with a previous study by Mamudu et al (19). Total coronary calcium is commonly used to assess the risk of future atherosclerosis. The CAC is currently used as a screening test in some population subgroups, especially in some Asian countries. Although this method provides a valuable assessment in determining the pathophysiology of cardiovascular disease (20), it is not yet clear whether this method can be associated with better outcomes in the clinic than other assessment methods. A study in 2018 showed that CAC, like mammography used to diagnose breast cancer, is a powerful method for assessing the risk of cardiovascular disease, however, it cannot yet be suggested as a screening and requires further studies(6).

## Conclusion

The primary results of this study showed that more than half of patients in CAC screening had CAC = 0. Diabetes and smoking were the significant predictors in CAC > 0. Overall, health condition and a family history of CHD was associated with CAC > 0, and CACS is a marker for risk factors associated with atherosclerosis. This study found that scanning those with a CAC > 0 scores may allow for more accurate CHD risk updates.

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### *Conflict of Interests*

The authors declare that they have no competing interests.

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