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**Research Article** 



# The Relationship Between the Severity of Coronary Artery Calcification and Aortic Artery Calcification in Iran

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#### Abstract

**Background:** The calcification of various coronary arteries is associated with the presence of calcification in other parts of the cardiovascular system, such as heart valves and different sections of the aorta.

**Objectives:** This study aimed to evaluate the correlation between the severity of coronary artery calcification and aortic artery calcification.

**Methods:** This cross-sectional study was conducted on patients suspected of having coronary artery disease who were candidates for chest computed tomography scanning. The calcium score in the coronary arteries, the aortic artery, and the mitral and aortic valves was assessed using the Agatston method.

**Results:** In examining the relationship between the frequency of aortic calcification and the severity of coronary artery calcification, none of the patients without calcification or with minimal coronary calcification had calcification in any segment of the aortic artery. Among patients with mild, moderate, severe, and very severe coronary calcification, the frequency of aortic arch calcification was 5%, 12%, 8%, and 25%, respectively, and the frequency of ascending aorta calcification was 0%, 5%, 5%, and 10%, respectively. The frequency of descending aorta calcification was 10%, 10%, 15%, and 25%, respectively. Overall, a significant correlation was observed between the frequency of coronary artery and aortic artery calcification (P = 0.008). Additionally, the severity of coronary artery calcification was significantly correlated with the mean score of aortic artery calcification (P = 0.001).

**Conclusions:** The presence of calcification in the coronary arteries is accompanied by the progression of calcification in various parts of the aorta.

Keywords: Coronary Artery Calcification, Aortic Artery Calcification, Coronary Artery Disease, Agatston Score

### 1. Background

Coronary heart disease is a major global cause of mortality, with atherosclerosis being the primary underlying condition, leading to the formation of calcified plaques. The burden of coronary atherosclerosis is quantitatively assessed through calcium scoring, a well-established parameter in computed tomography (CT) imaging of coronary arteries. Various studies have identified the coronary artery calcification score as an independent and robust predictor of morbidity and mortality related to coronary atherosclerotic diseases (1-6). Calcification can occur not only in arterial vessels but also in the aortic and mitral valves, both of which can be evaluated using CT techniques.

Despite the potential clinical significance, coronary CT studies often do not include assessments of aortic and mitral valve calcium scores. It has been reported that the aortic valve calcium score is strongly correlated

Copyright © 2024, Annals of Military and Health Sciences Research. This open-access article is available under the Creative Commons Attribution-NonCommercial 4.0 (CC BY-NC 4.0) International License (https://creativecommons.org/licenses/by-nc/4.0/), which allows for the copying and redistribution of the material only for noncommercial purposes, provided that the original work is properly cited. with aortic stenosis (5). Aortic stenosis is the third most prevalent cardiovascular disease, following coronary artery disease and hypertension, with an increasing incidence in Asia and other regions due to rising life expectancy. Mitral valve calcification, on the other hand, has been associated with an elevated risk of stroke, atrial fibrillation, and cardiovascular mortality (6-8). Research into the pathophysiology of aortic and mitral valve calcification remains an active area of investigation. However, studies have shown that valve calcification and coronary atherosclerosis share similar risk factors (9-11).

Coronary atherosclerosis occurs when the lining of the heart's blood vessels becomes dysfunctional, leading to the activation of chronic inflammatory factors. Similarly, histopathological studies have identified endothelial damage and inflammation in calcified aortic and mitral valves (12). These findings suggest that the mechanisms underlying coronary artery, aortic, and mitral valve calcification may overlap. Despite the similarities in the literature regarding these calcifications, the precise relationship between coronary artery calcification and calcifications in the aorta or mitral valve remains unclear.

#### 2. Objectives

The present study aimed to investigate the correlation between coronary artery calcification scores and aortic artery calcification, as well as calcification in the mitral and aortic valves. This research seeks to contribute to the understanding of the shared and distinct mechanisms underlying these forms of calcification.

# 3. Methods

### 3.1. Study Population

This cross-sectional study was conducted with patients consecutively referred to Modarres Hospital in Tehran with suspected coronary artery disease, who were evaluated using chest CT scanning. Exclusion criteria included low image quality, a history of any coronary or valvular diagnostic or therapeutic intervention, a history of heart valve diseases, endocarditis, or any type of cardiomyopathy, a history of congenital heart disorders, and the presence of any abnormal morphology in the aorta or heart valves. The various stages of this project were approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1403.077).

# 3.2. Study Assessments

Initially, through patient interviews, background information, including demographic characteristics, was collected. The study checklist documented participants' medical history, including hypertension, diabetes, hyperlipidemia, family history of heart disease, and history of smoking or opium use. Patients underwent chest CT evaluation, and the calcium score in the coronary arteries, aortic artery (at different sections), and the mitral and aortic valves was determined using the Agatston method with Syngo.via software. All imaging was conducted by an experienced radiologist with over 10 years of expertise in imaging.

The calcium score for the aortic valve was measured from the sinotubular junction to the aortic valve leaflets, while the mitral valve calcium score was assessed between the left atrium and left ventricle, including the leaflets. All measurements were performed by the radiologist to ensure consistency and accuracy. Finally, the correlation between the coronary artery calcification score and the calcification scores at the three positions—the aortic artery, aortic valve, and mitral valve—was analyzed.

### 3.3. Statistical Analysis

Quantitative data were expressed as mean ± standard deviation (SD), while categorical variables were presented as percentages. The chi-square test was employed to compare qualitative variables. Data analysis was performed using SPSS software, version 23, and a significance level of less than 0.05 was considered statistically significant.

## 4. Results

A total of 100 patients were included in the study, with a mean age of  $60.9 \pm 6.6$  years, of whom 70% were male. The mean Body Mass Index (BMI) was  $28.2 \pm 2.5$  kg/m<sup>2</sup>. Regarding cardiovascular risk factors, the prevalence of hypertension was 38%, diabetes was reported in 30% of patients, hyperlipidemia was present in 26%, and 15% were current smokers. Additionally, 35% of the patients had a family history of ischemic heart

disease. The baseline characteristics and laboratory marker statuses are detailed in Table 1.

Variables	Values
Average age (y)	$60.9\pm6.6$
Average BMI, Kg/m <sup>2</sup>	$28.2\pm2.5$
Hypertension	38
Diabetes mellitus	30
Hyperlipidemia	26
Smoking	15
Family history of ischemic heart disease	0.35
Status of laboratory markers	
Average serum triglyceride level, mg/dL	$135\pm45$
Mean serum total cholesterol, mg/dL	$220\pm\!18$
Mean serum HDL level, mg/dL	$44\pm11$
Mean serum LDL level, mg/dL	$130\pm30$
Mean serum hemoglobin level, mg/dL	$12.2\pm1.0$
Mean serum CRP level, mg/dL	$0.15\pm0.10$
Abbreviation: BMI, Body Mass Index.	
<sup>a</sup> Values are expressed as mean $\pm$ SD or %.	

Based on CT scan findings, aortic arch calcification was observed in 50% of patients, ascending aortic calcification in 20%, descending aortic calcification in 60%, aortic valve calcification in 18%, and mitral valve calcification in 3%. The mean calcium scores were 390 for the aortic arch, 52 for the ascending aorta, 565 for the descending aorta, and 529 for the coronary arteries.

Among the 100 patients studied, 18% had no coronary artery calcification (CAC = 0), 4% had minimal calcification, 20% had mild calcification, 15% had moderate calcification, 18% had severe calcification, and 25% had extreme calcification.

An analysis of the relationship between aortic calcification frequency and coronary artery calcification severity (Table 2) revealed that none of the patients without calcification or with minimal coronary calcification exhibited calcification in any position of the aortic artery. Among patients with mild, moderate, severe, and extreme coronary calcification, the frequency of aortic arch calcification was 5%, 12%, 8%, and 25%, respectively. The frequency of ascending aorta calcification was 0%, 5%, 5%, and 10%, respectively, while the frequency of descending aorta calcification was 10%, 10%, 15%, and 25%, respectively. Overall, a significant relationship was found between the frequency of

coronary artery calcification and aortic artery calcification (P = 0.008).

Similarly, when evaluating the relationship between the average score of aortic calcification and the severity of coronary artery calcification (Table 3), it was observed that none of the patients without calcification or with minimal coronary calcification exhibited calcification in any position of the aortic artery. Among patients with mild, moderate, severe, and very severe coronary calcification, the mean score of aortic arch calcification was 36, 60, 700, and 1300, respectively. The mean score of ascending aorta calcification was 0, 50, 200, and 400, respectively, while the mean score of descending aorta calcification was 150, 400, 900, and 1500, respectively. There was a significant correlation between the severity of coronary artery calcification and the average score of aortic artery calcification (P = 0.001) (Table 3).

#### 5. Discussion

The present study was designed and conducted to evaluate the relationship between coronary artery calcification and calcification in other parts of the cardiovascular system, such as the aorta. This investigation was based on the assumption that calcification can occur simultaneously across various regions of the cardiovascular system, a concept of critical importance for radiological interpretation and the assessment of vascular involvement severity. Our findings demonstrate that the severity of coronary artery calcification correlates with the severity and extent of calcification in different segments of the aorta. Specifically, both the number of calcified points and the scores indicating the intensity of involvement align closely between the coronary arteries and the aorta.

Recent studies suggest that calcification in various coronary arteries is associated with calcification in other cardiovascular regions, including heart valves and different sections of the aorta. The calcification process appears to follow a similar pathophysiology across these regions, leading to concurrent events in multiple areas of the cardiovascular system. According to research, this similarity arises from the shared underlying risk factors for cardiovascular diseases that predispose all parts of the cardiovascular system to calcification.

In our study, we explored the relationship between coronary artery calcification and the severity of aortic artery calcification. Notably, none of the patients without coronary artery calcification exhibited

Zone	None	Minimal	Mild	Moderate	Severe	Extreme	P-Value
Aortic arch	0	0	5	12	8	25	
ascending aorta	0	0	0	5	5	10	0.008
Descending aorta	0	0	10	10	15	25	
Values are expressed as %							
values are expressed as 10.							
The analysis was performed by t	he chi-square test.						
The analysis was performed by t	he chi-square test.	cion Severity and Aor	tic Calcification	Score			
The analysis was performed by t able 3. Relationship Between Co Zone	he chi-square test. ronary Artery Calcifical <b>None</b>	tion Severity and Aor Minimal	tic Calcification Mild	Score Moderate	Severe	Extreme	P-Value
The analysis was performed by t able 3. Relationship Between Co Zone Aortic arch	he chi-square test. ronary Artery Calcificat None 0	tion Severity and Aor Minimal 0	tic Calcification Mild 36	Score Moderate 60	<b>Severe</b> 700	Extreme 1300	P-Value
The analysis was performed by t able 3. Relationship Between Co Zone Aortic arch ascending aorta	he chi-square test. ronary Artery Calcificat None 0 0	tion Severity and Aor Minimal 0 0	tic Calcification Mild 36 0	Score Moderate 60 50	<b>Severe</b> 700 200	<b>Extreme</b> 1300 400	<b>P-Value</b> 0.001

calcification in any part of the aorta. Conversely, the frequency and score of calcification in various segments of the aorta increased proportionally with the severity of coronary artery calcification. Specifically, greater calcification in the coronary arteries was associated with increased calcification in the aortic arch, ascending aorta, and descending aorta.

This finding is significant because the presence of coronary artery calcification can serve as a reliable predictor of calcification and, consequently, the activation of the atherosclerotic process in different parts of the aorta. Similarly, the presence of aortic calcification could predict coronary artery involvement, emphasizing the interconnected nature of calcification within the cardiovascular system.

Such a relationship has also been demonstrated in previous studies, although not all have confirmed a statistically significant association. In the study by Suwita et al., a significant but weak correlation was observed between coronary artery calcium scores and aortic artery calcium scores (13). Similarly, Hata et al. found that among different sections of the aorta, the highest calcification frequency occurred in the aortic arch (77.4%). Significant coronary artery calcification was observed in 39.1% of cases, and calcification in various areas of the aorta and aortic valve was significantly associated with coronary artery calcification, even after adjusting for cardiovascular risk factors and statin use (14). In the study by Allison et al., adjustments for age, gender, and cardiovascular risk factors revealed that individuals with calcification in the thoracic aorta had the highest likelihood of annular calcium, while those with calcification in the abdominal aorta were more likely to have mitral valve calcification. Calcium increases in the abdominal and iliac aorta were significantly associated with calcium in the aortic annulus, and calcification in the thoracic aorta was significantly linked to calcium in the mitral annulus (15). This study underscored that calcification occurring in one part of the aorta is often related to calcification in other regions, with a widespread and simultaneous pattern of involvement across different areas.

More intriguingly, some studies have shown that calcification in the aorta may coincide with calcification in other vascular systems, such as the cervical and cerebral arteries (16). This suggests that calcification is a systemic phenomenon. Once the process is activated, it is not confined to a single area of the cardiovascular system. Instead, activation in one part can lead to widespread involvement in other regions. Therefore, understanding and identifying calcification in one part of the cardiovascular system could have broader implications for predicting and managing calcification in other areas.

#### 5.1. Conclusions

As a final conclusion, our study demonstrated that the occurrence of calcification in the aorta (observed in

82% of cases) was associated with a 20 - 60% prevalence of calcification in various segments of the aorta. This finding highlights that calcification in the coronary arteries is closely and simultaneously accompanied by the progression of calcification in different sections of the aorta. Furthermore, our results revealed a strong correlation between the severity of coronary artery calcification and both the frequency and score of calcification in the aorta. This underscores the systemic and simultaneous nature of calcification, indicating that calcification in one part of the cardiovascular system often reflects widespread involvement in other regions.

### Footnotes

**Authors' Contribution:** Conception and design and supervision: T. F. L., and H. K.; data analysis: H. K., and T. F. L.; drafting of the manuscript: N. R. P., and A. T.; administrative, technical support: M. K. K., and A. T.

**Conflict of Interests Statement:** The authors declare that they have no conflict of interest.

**Data Availability:** The dataset presented in the study is available on request from the corresponding author during submission or after its publication. The data are not publicly available due to patient's privacy.

**Ethical Approval:** Research Ethics Committees of School of Medicine-Shahid Beheshti University of Medical Sciences approved the study (IR.SBMU.MSP.REC.1403.077 ).

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**Informed Consent:** All participants provided informed consent.

#### References

- Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation*. 2018;137(12):e67-e492. [PubMed ID: 29386200]. https://doi.org/10.1161/CIR.000000000000558.
- Neves PO, Andrade J, Moncao H. Coronary artery calcium score: current status. *Radiol Bras.* 2017;**50**(3):182-9. [PubMed ID: 28670030]. [PubMed Central ID: PMC5487233]. https://doi.org/10.1590/0100-3984.2015.0235.
- Ohira T, Iso H. Cardiovascular disease epidemiology in Asia: an overview. Circ J. 2013;77(7):1646-52. [PubMed ID: 23803294].

#### https://doi.org/10.1253/circj.cj-13-0702.

- Ambrose JA, Singh M. Pathophysiology of coronary artery disease leading to acute coronary syndromes. *F1000Prime Rep.* 2015;7:8. [PubMed ID: 25705391]. [PubMed Central ID: PMC4311268]. https://doi.org/10.12703/P7-08.
- Shimizu K, Yamamoto M, Koyama Y, Kodama A, Sato H, Kano S, et al. Usefulness of routine aortic valve calcium score measurement for risk stratification of aortic stenosis and coronary artery disease in patients scheduled cardiac multislice computed tomography. *Int J Cardiol Heart Vasc.* 2015;9:95-9. [PubMed ID: 28785716]. [PubMed Central ID: PMC5497337]. https://doi.org/10.1016/j.ijcha.2015.10.008.
- Zsuzsanna S, Theodora B, Beáta J, I B. Correlations Between Severity of Coronary Calcification and Impairment of Left Ventricular Ejection Fraction. Acta Medica Marisiensis. 2013;59(5):267-9. https://doi.org/10.2478/amma-2013-0062.
- Lerman DA, Prasad S, Alotti N. Calcific Aortic Valve Disease: Molecular Mechanisms and Therapeutic Approaches. *Eur Cardiol.* 2015;**10**(2):108-12. [PubMed ID: 27274771]. [PubMed Central ID: PMC4888946]. https://doi.org/10.15420/ecr.2015.10.2.108.
- Lindman BR, Clavel MA, Mathieu P, Iung B, Lancellotti P, Otto CM, et al. Calcific aortic stenosis. *Nat Rev Dis Primers*. 2016;2:16006. [PubMed ID: 27188578]. [PubMed Central ID: PMC5127286]. https://doi.org/10.1038/nrdp.2016.6.
- Tay ELW, Ngiam JN, Kong WK, Poh KK. Management of severe aortic stenosis: the Singapore and Asian perspective. *Singapore Med J.* 2018;**59**(9):452-4. [PubMed ID: 30128576]. [PubMed Central ID: PMC6158140]. https://doi.org/10.11622/smedj.2018103.
- Pasipoularides A. Calcific Aortic Valve Disease: Part 1-Molecular Pathogenetic Aspects, Hemodynamics, and Adaptive Feedbacks. J Cardiovasc Transl Res. 2016;9(2):102-18. [PubMed ID: 26891845]. [PubMed Central ID: PMC4833551]. https://doi.org/10.1007/s12265-016-9679-z.
- Koulaouzidis G, Nicoll R, MacArthur T, Jenkins PJ, Henein MY. Coronary artery calcification correlates with the presence and severity of valve calcification. *Int J Cardiol.* 2013;**168**(6):5263-6. [PubMed ID: 23993324]. https://doi.org/10.1016/j.ijcard.2013.08.019.
- Massera D, Trivieri MG, Andrews JPM, Sartori S, Abgral R, Chapman AR, et al. Disease Activity in Mitral Annular Calcification. *Circ Cardiovasc Imaging*. 2019;**12**(2). e008513. [PubMed ID: 30712363]. [PubMed Central ID: PMC6366554]. https://doi.org/10.1161/CIRCIMAGING.118.008513.
- Suwita BM, Suroyo I, Rusdi L, Prihartono J. The correlation between coronary artery, aortic, and mitral valve calcification in patients with coronary atherosclerosis. *Egypt J Radiol Nuclear Med.* 2023;**54**(1). https://doi.org/10.1186/s43055-023-01053-6.
- Hata Y, Mochizuki J, Okamoto S, Matsumi H, Hashimoto K. Aortic calcification is associated with coronary artery calcification and is a potential surrogate marker for ischemic heart disease risk: A crosssectional study. *Med (Baltimore)*. 2022;**101**(29). e29875. [PubMed ID: 35866765]. [PubMed Central ID: PMC9302345]. https://doi.org/10.1097/MD.000000000029875.
- Allison MA, Cheung P, Criqui MH, Langer RD, Wright CM. Mitral and aortic annular calcification are highly associated with systemic calcified atherosclerosis. *Circulation*. 2006;113(6):861-6. [PubMed ID: 16461818]. https://doi.org/10.1161/CIRCULATIONAHA.105.552844.
- 16. Mostowik M, Palka I, Gajos G, Nessler J, Gackowski A. Mitral and aortic annular calcifications and cerebrovascular ischemic episodes in

patients with coronary artery disease. *Pol Arch Med Wewn*. 2014;**124**(7-8):373-9. [PubMed ID: 24882430]. https://doi.org/10.20452/pamw.2343.