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Correlation between Aortic Valve and Mitral Valve Calcification and Coronary Artery Disease by Using Computed Tomography Coronary Angiography

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ABSTRACT

Background: Aortic valve calcification (AVC) and mitral annular calcification (MAC) are chronic degenerative processes frequently observed in elderly individuals and often coexist with coronary artery disease (CAD). The association between valvular calcification and CAD remains an area of ongoing investigation.

Objective: This study aims to assess the correlation between AVC and MAC with the presence and severity of CAD using computed tomography coronary angiography (CTCA).

Patients and methods: This prospective cross-sectional study included 100 patients (age 58–85 years) with echocardiographic evidence of AVC and/or MAC who underwent CTCA for suspected ischemic heart disease (IHD). Quantification of AVC was performed using the Agatston score, whereas MAC was categorized based on a predefined four-grade scale. Coronary artery lesions were classified based on the degree of stenosis.

Results: Significant AVC demonstrated a robust association with CAD, present in 84.2% of cases compared to 8.3% without AVC ($P < 0.001$), and was most notably correlated with LAD artery involvement (93.9% vs. 11.8%, $P < 0.001$). Patients with significant AVC had a higher prevalence of single-vessel (60.6% vs. 29.4%) and multiple-vessel disease (36.4% vs. 5.9%) ($P < 0.001$). MAC was not substantially associated with CAD presence ($P = 0.417$), but severe/diffuse MAC correlated with multi-vessel disease (87.5%, $P < 0.001$).

Conclusion: AVC was significantly associated with CAD, particularly LAD involvement, while MAC was linked to multi-vessel disease in severe cases. These findings highlight the potential role of valvular calcification as an imaging marker for CAD risk stratification.

Keywords: Aortic valve calcification, Coronary artery disease, Mitral annular calcification, Computed tomography coronary angiography.

INTRODUCTION

Calcification of the aortic and mitral valves represents a chronic and progressive degenerative condition, marked by gradual, age-related deterioration of the valve leaflets without significant inflammatory involvement. This process involves passive calcium deposition, leading to leaflet thickening and stiffness. It is most commonly observed in older adults, particularly those aged 65 years and above [1].

Valvular calcification and coronary artery disease (CAD) are cardiovascular conditions that frequently coexist and share common risk factors, including advanced age, male sex, uncontrolled diabetes mellitus (DM), hypertension (HTN), cerebrovascular disease, smoking, dyslipidemia, obesity, a sedentary lifestyle, chronic kidney disease (CKD), and a family history of cardiovascular disease (CVD) [2,3].

A strong relationship has been established between aortic and mitral valve calcification and CAD. Earlier pathological investigations have identified foam cells—hallmarks of early atherosclerotic changes—on the endothelial surfaces of coronary arteries, the aortic aspects of the aortic valve cusps, and the ventricular aspect of the posterior mitral leaflet [4].

Moreover, evidence from histopathological studies reveals that aortic valve sclero-calcification (AVSC) exhibits characteristics akin to those of atherosclerotic lesions, supporting the notion that it may be regarded as a distinct form of atherosclerosis [5-7].

Among the best non-invasive cardiac imaging modalities for assessing valvular calcification is computed tomography coronary angiography (CTCA). This imaging technique is also a valuable diagnostic tool for evaluating suspected CAD. CAD can be assessed using contrast-enhanced imaging, with lesion severity determined based on the percentage of coronary stenosis. Additionally, aortic valve calcification can be quantified using the Agatston score, while mitral valve calcification is evaluated using a four-point grading scale [8,9].

This study aims to investigate the correlation between AVC and MAC with the presence and severity of CAD using CTCA.

PATIENTS AND METHODS

Design and population

Conducted at Ain Shams University's Cardiology Department, this prospective cross-sectional study included 100 elderly patients exhibiting manifestations suggestive of ischemic heart disease (IHD). All patients were scheduled to undergo CTCA to assess myocardial ischemia.

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Inclusion criteria

Patients aged 50–90 years with echocardiographic findings consistent with calcification of both the aortic and mitral valves, and who were scheduled for CT coronary angiography to evaluate for IHD, were enrolled in the study.

Exclusion criteria

Patients diagnosed with acute coronary syndrome, including NSTEMI, STEMI, or unstable angina, were excluded. Those with a history of coronary angiography, coronary stenting, coronary artery bypass surgery, pacemaker implantation, or defibrillator implantation were also excluded. Other exclusion criteria included a history of rheumatic heart disease, balloon angioplasty, prosthetic valve replacement, or congenital heart disease. Patients with renal insufficiency (estimated GFR <30 ml/min/1.73 m²), irregular cardiac rhythms (such as atrial fibrillation or frequent PVCs), or impaired left ventricular systolic function (EF <30%) were not eligible. Additionally, patients with a known allergy to iodinated contrast agents were excluded.

METHODS

Each patient underwent a comprehensive clinical evaluation, including a full personal history and transthoracic echocardiography (TTE) using the Vivid E95 echocardiography machine. Prior to the CT examination, patients were well-prepared through proper hydration, continuous ECG and blood pressure (BP) monitoring, and ensuring a resting heart rate (HR) below 70 beats per minute. Patients were advised to fast for 4–6 hours and to avoid caffeine intake for at least 12 hours before the test. They were also instructed on the breathing maneuver required during the procedure.

A non-contrast CT scan was first performed to assess aortic valve calcification using the Agatston score and mitral valve calcification using a four-point scale. This was followed by contrast-enhanced coronary angiography using a TOSHIBA 64-slice CT scanner to investigate the presence and severity of coronary artery lesions. The four major coronary arteries assessed included the right coronary artery (RCA), left main coronary artery (LMCA), the left circumflex artery (LCX), and the left anterior descending artery (LAD).

CT Coronary Angiography Analysis

Quantification of aortic valve calcification was performed via the Agatston method, wherein the area of calcification is multiplied by a density factor determined by the highest Hounsfield unit (HU) value within that area. Lesions were assigned a density score according to their peak HU values as follows: 1 for 130–199 HU, 2 for 200–299 HU, 3 for 300–399 HU, and 4 for lesions with a maximal density greater than 400 HU. Aortic valve calcification was considered significant when it exceeded 1600 HFU in males and 1200 HFU in females [4].

A semiquantitative four-point system was employed to grade mitral valve calcification: score 0 for absence of calcification, score 1 for minimal spot-like deposits, score 2 for marked yet restricted calcification, and score 3 for extensive, severe calcific changes involving both the anterior and posterior mitral leaflets [10].

Based on the percentage of luminal stenosis, the severity of coronary artery lesions was classified into five categories: Grade 0 (no plaque, no luminal stenosis), Grade 1 (minimal plaque with <25% luminal stenosis), Grade 2 (mild plaque with 25–49% stenosis), Grade 3 (moderate plaque with 50–69% stenosis), and Grade 4 (severe plaque with 70–99% stenosis).

Ethical considerations:

Ethical approval for this study was granted by the Research Ethics Committee at Ain Shams University. Prior to enrollment, all participants signed a written informed consent form, which detailed the nature and purpose of the study, as well as their authorization for data usage in publication. Measures were taken to ensure participants' privacy and confidentiality. The study was conducted in full accordance with the ethical standards of the World Medical Association's Declaration of Helsinki concerning research involving human subjects.

Statistical analysis

All statistical analyses were carried out using SPSS software, version 28 (IBM, Armonk, NY, USA). Frequencies and percentages were used to summarize categorical variables. The Chi-square or Fisher's exact test was used for analyzing categorical variables. Statistical significance was defined as a two-tailed P-value below 0.05.

RESULTS

Patients with significant aortic valve calcification had a substantially greater occurrence of CAD relative to those without significant calcification (84.2% vs. 8.3%). Conversely, non-significant aortic valve calcification was more common among patients without CAD (91.7% vs. 15.8%) **(Table 1)**.

Table 1: **Correlation between aortic valve calcification in relation to the presence of coronary artery disease**

	Coronary vessel disease		
	Yes (n =76)	**No (n = 24)**	**P-value**
Aortic valve calcification			
Significant	64 (84.2)	2 (8.3)	**<0.001***
Non-Significant	12 (15.8)	22 (91.7)	

n: number, *: Significant P-value.

Patients with significant aortic valve calcification had a greater incidence of LAD artery disease relative to those with non-significant calcification (93.9% vs. 11.8%). A greater proportion of LCX artery involvement was detected in patients with pronounced aortic valve calcification (24.2% vs. 5.9%). No substantial association was found between aortic valve calcification and RCA disease **(Table 2)**.

Table 2: Correlation between aortic valve calcification and affected coronary artery disease

	Aortic valve		
	Significant (n =66)	**Non-Significant (n =34)**	**P-value**
LAD	62 (93.9)	4 (11.8)	**<0.001***
LCX	16 (24.2)	2 (5.9)	**0.028***
RCA			
Significant	16 (24.2)	8 (23.5)	0.937
Non-Significant	50 (75.8)	26 (76.5)	

n: number, LAD: Left Anterior Descending artery, LCX: Left Circumflex artery, RCA: Right Coronary Artery, *: Significant P-value.

Patients exhibiting significant aortic valve calcification demonstrated a markedly higher prevalence of single-vessel CAD relative to those without significant calcification (60.6% vs. 29.4%). Additionally, the occurrence of multi-vessel disease was more frequent in the significant calcification group (36.4% vs. 5.9%). On the other hand, the absence of atherosclerotic disease was observed at a markedly higher rate in those with non-significant aortic valve calcification (64.7% vs. 3%) **(Table 3)**.

Table3: Correlation between aortic valve calcification and number of the affected coronary artery disease

	Aortic valve		
	Significant (n =66)	**Non-Significant (n =34)**	**P-value**
Affected vessel			
Single	40 (60.6)	10 (29.4)	**<0.001***
Multiple	24 (36.4)	2 (5.9)	
NAD	2 (3)	22 (64.7)	

n: number, NAD: No Atherosclerotic Disease, *: Significant P-value.

No substantial correlation was found between mitral valve calcification and the presence of CAD **(Table 4)**.

Table 4. Correlation between Mitral valve calcification and presence of coronary artery disease

	Mitral valve				
	No (n =22)	**Minor (n =34)**	**Marked (n =28)**	**Diffuse (n =16)**	**P-value**
Yes	16 (72.7%)	24 (70.6%)	22 (78.6%)	14 (87.5%)	0.417
No	6 (27.3%)	10 (29.4%)	6 (21.4%)	2 (12.5%)	

n: number.

Patients with extensive mitral valve calcification demonstrated a significantly higher prevalence of multi-vessel coronary artery disease compared to other groups (87.5%). Notably, none of the individuals in this group exhibited single-vessel disease. No atherosclerotic disease was more frequent in patients with no or minor mitral valve calcification **(Table 5)**.

Table 5: Correlation between mitral valve calcification and number of affected coronary arteries

	Mitral valve				
	No (n =22)	**Minor (n =34)**	**Marked (n =28)**	**Diffuse (n =16)**	**P-value**
Affected vessels					
Single	14 (63.6%)	18 (52.9%)	18 (64.3%)	0 (0%)	**<0.001***
Multiple	2 (9.1%)	6 (17.6%)	4 (14.3%)	14 (87.5%)	
NAD	6 (27.3%)	10 (29.4%)	6 (21.4%)	2 (12.5%)	

n: number, NAD: No Atherosclerotic Disease, *: Significant P-value.

DISCUSSION

Aortic and mitral valve calcification is considered a manifestation of atherosclerotic heart disease [11]. Data from recent epidemiological investigations indicate that the combined manifestation of AVC and MAC is progressive over time and may serve as a reliable marker for identifying patients at increased risk of CVD. Moreover, the coexistence of AVC and MAC has been shown to be more strongly associated with cardiovascular mortality than either condition alone [12].

Our study revealed a statistically significant higher prevalence of aortic valve calcification in subjects with significant CAD compared to those with non-significant CAD (84.2% vs. 8.3%; $P < 0.05$). **Aronow *et al.*** [13] corroborated these observations, showing that aortic valve sclerosis, characterized by cusp thickening or calcification in older adults, was associated with a 1.8-fold increased risk of coronary events. They recommended screening these patients for CAD.

Conversely, our study found no significant correlation between mitral valve calcification and the presence of CAD ($P > 0.05$). In contrast, **Aronow *et al.*** [13] suggested that MAC in elderly should alert physicians to the potential presence of cardiovascular atherosclerosis (42% vs. 26%; $P < 0.05$) and found that MAC was associated with a higher prevalence of multi-vessel disease (≥2-vessel disease: 19% vs. 7%; $P = 0.02$).

This discrepancy may be explained by differences in diagnostic methodology, as our study utilized MSCT, while **Adler *et al.*** [14] relied on echocardiography. Additionally, the relatively small number of patients with significant MAC in our study may have contributed to the variation in findings.

Our results also demonstrated a highly significant association between AVC and single-vessel disease, specifically involving the LAD ($P < 0.05$). **Geerlings-Batt *et al.*** [15] further supported this association, reporting that isolated left CAD is more frequently linked to AVC, while isolated right CAD is more commonly associated with MAC.

While the study provides valuable insights, certain limitations must be considered. The relatively small number of participants may constrain the generalizability of the findings. Moreover, conducting the study at a single center may introduce selection bias and limit the diversity of the study population. Third, while we utilized MSCT for assessing calcifications, other imaging modalities such as echocardiography or intravascular ultrasound might have provided additional insights, particularly in detecting early-stage calcifications. Additionally, we did not account for potential confounding factors such as inflammatory markers, genetic predisposition, or medication use, which could influence the progression of AVC and MAC. Finally, the cross-sectional study design precludes the ability to establish causality between calcification and CAD, highlighting the need for longitudinal studies to confirm our findings.

CONCLUSION

AVC was significantly associated with CAD, particularly LAD involvement, while MAC was linked to multi-vessel disease in severe cases. These findings highlight the potential role of valvular calcification as an imaging marker for CAD risk stratification.

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Conflict of interest: None.

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