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ORIGINAL ARTICLE

Subclinical systolic left ventricular dysfunction in patients with non-significant coronary artery stenosis detected by coronary computed tomography (CT) angiography

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ABSTRACT

Aim To investigate the relationship between coronary artery calcium (CAC) score and left ventricular global longitudinal strain (LV GLS) in patients with arterial hypertension who had a negative treadmill exercise stress test but mild to intermediate coronary stenosis on coronary computed tomography angiography (CCTA).
Methods A total of 53 hypertensive patients (mean age 54.8 ± 4.8 years; 50.9% male) with 30–50% coronary stenosis on CCTA were included. Patients with diabetes, malignancy, or established coronary/peripheral artery disease were excluded. CAC score, left ventricular ejection fraction (LVEF, Simpson's method), and LV GLS (speckle-tracking echocardiography) were measured. Groups were stratified by GLS (< 18.5% vs. ≥ 18.5%) and LVEF (< 60% vs. ≥ 60%), and CAC score differences were assessed using the Mann–Whitney U test.
Results The median CAC score was 27 (IQR 16–44.5), median LVEF 60% (IQR 58–63%), and mean GLS 19.37 ± 0.89%. No overall association was found between CAC score and LV function by LVEF or GLS. In patients with left anterior descending (LAD) stenosis (30–50%), reduced LV function was linked to significantly higher CAC score. Median CAC score was higher in patients with GLS ≤ 18.5% (157 vs. 44.5; $p = 0.019$) and LVEF <60% (157 vs. 44.5; $p = 0.019$). No significant associations were found in right coronary artery (RCA), circumflex artery (Cx), or three-vessel stenosis subgroups.
Conclusion Higher CAC score in hypertensive patients with mild LAD stenosis and negative stress testing identify those at risk of subclinical LV dysfunction.

Keywords: coronary artery calcium score, coronary artery disease, global longitudinal strain, left anterior descending

INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality worldwide, encompassing a broad clinical spectrum from stable angina to acute myocardial infarction and sudden cardiac death. The early detection of CAD remains challenging (1). In the early stages, anatomical changes in the coronary arteries may not cause significant hemodynamic obstruction; thus, conventional noninvasive tests such as treadmill stress testing and evaluation of left ventricular ejection fraction (LVEF) usually remain within normal limits (2–4).

Increasing evidence suggests that even mild coronary lesions may have functional consequences on the myocardium, especially on the subendocardial longitudinal fibres, which are most sensitive to ischemia. These subtle alterations can be detected by speckle-tracking echocardiography using global longitudinal strain (GLS), allowing for the identification of subclinical systolic left ventricular (LV) dysfunction before a measurable decline in LVEF occurs (1,5–7).

Coronary artery calcium (CAC), quantified by computed tomography, serves as a robust marker of total atherosclerotic burden and a predictor of cardiovascular risk (8–11).

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According to the 2024 European Society of Cardiology (ESC) Guidelines for the management of chronic coronary syndromes (CCS), coronary computed tomography angiography (CCTA) is recommended as a first-line anatomical imaging test in patients with low to intermediate pre-test probability of obstructive CAD, due to its high negative predictive value and ability to detect both obstructive and non-obstructive coronary atherosclerosis (12). Guidelines emphasize that the presence of coronary atherosclerosis, irrespective of stenosis severity, represents a chronic disease process associated with increased cardiovascular risk. In addition, coronary microvascular dysfunction is recognized as an important cause of myocardial ischemia in patients without obstructive CAD (12). In this context, symptomatic patients with evidence of coronary atherosclerosis on CCTA and negative functional testing may be considered within the spectrum of CCS, even in the absence of hemodynamically significant stenosis; however, such patients are often classified as low risk and managed conservatively (3,12).

Nevertheless, the association between CAC score and early LV functional impairment in patients with mild to moderate coronary stenosis and negative stress testing remains unclear.

The aim of this study was to evaluate the relationship between CAC score and subclinical systolic LV dysfunction assessed by GLS in patients with non-significant coronary stenosis (30–50%) detected by coronary CT angiography.

PATIENTS AND METHODS

Patients and study design

This observational, cross-sectional study with retrospective patient identification included 53 patients with arterial hypertension evaluated at General Hospital "Prim. dr. Abdulah Nakaš" during May 2025. Patients were retrospectively identified based on prior CCTA performed at multiple institutions between October 2024 and May 2025 for suspected CAD despite previously negative treadmill exercise testing. Only patients with mild to moderate coronary artery stenosis (30–50%) confirmed on CCTA were eligible for inclusion. Patients with a history of coronary or peripheral arterial disease, diabetes mellitus, or malignancy were excluded.

Data collected included age, sex, CAC score, CCTA findings (location and extent of coronary stenosis), LVEF assessed by Simpson's biplane method, and LV GLS obtained using 2D speckle-tracking echocardiography (2D-STE).

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the institution's ethics committee.

Methods

Patients were stratified into two groups based on GLS (< 18.5% vs. ≥ 18.5%) (13) and LVEF (< 60% vs. ≥ 60%). In addition, the association between CAC score and LV systolic function parameters (LVEF and GLS) was assessed within subgroups based on the anatomical distribution of coronary stenosis (three-vessel disease, left anterior descending artery- LAD, right coronary artery- RCA, and circumflex artery- Cx stenosis).

Statistical analysis

Continuous variables were tested for normality using the Kolmogorov–Smirnov test and presented as mean±standard deviation (SD) or median (interquartile range, IQR), as appropriate. Differences in CAC scores between functional subgroups based on GLS and LVEF were analysed using the Mann–Whitney U test. A $p < 0.05$ was considered statistically significant.

RESULTS

The mean age of the study population was 54.8 ± 4.8 years, with 27 (50.9%) males. The median CAC score was 27 (IQR: 16–44.5). The median LVEF was 60% (IQR: 58–63%), and the mean GLS was 19.37 ± 0.89% (Table 1).

There were no significant differences in CAC scores between patients based on LVEF (< 60% vs. ≥ 60%; p = 0.792), nor based on GLS (≤ 18.5% vs. > 18.5%; p = 0.058) in the overall population.

Subgroup analysis among patients with LAD stenosis (30-50%) revealed that those with reduced LV function had significantly higher CAC scores. Those with GLS ≤ 18.5% had a significantly higher median CAC score compared to those with GLS > 18.5% (157 vs. 44.5; p = 0.019) (Figure 1). A comparable difference was observed in patients with LVEF < 60%, who also had a higher median CAC score than those with LVEF ≥ 60% (157 vs. 44.5; p = 0.019 (Figure 2).

Table 1. Demographic characteristics, calcium score, left ventricular functional parameters, and coronary artery involvement in hypertensive patients with mild to moderate coronary artery stenosis

Variable	Value
Mean age ±SD (interquartile range) (years)	54.79±4.77 (48–66)
Sex (No; %)	
Female	26 (49.1)
Male	27 (50.9)
Median Calcium score (interquartile range)	27 (16–44.5)
Median EFLV (interquartile range) (%)	60 (58–63)
GLS-LV (Mean±SD) (%)	19.37±0.89
	No.(%) of patients
Three-vessel disease (30–50%)	3 (5.7)
LAD (30–50%)	15 (28.3)
Cx (30–50%)	25 (47.2)
RCA (30–50%)	24 (45.3)

LVEF, left ventricular ejection fraction; GLS-LV, left ventricular global longitudinal strain; LAD, left anterior descending artery; Cx, circumflex artery; RCA, right coronary artery.

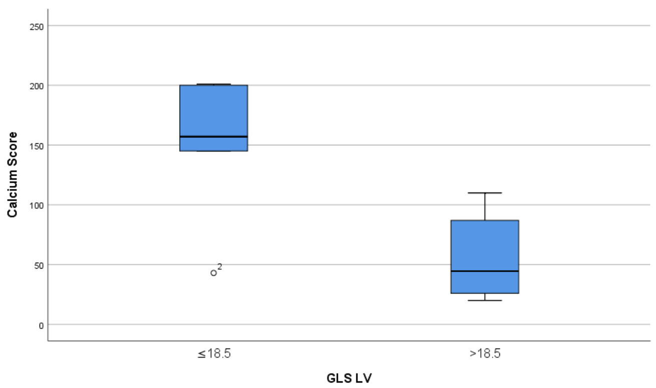

Figure 1. Distribution of calcium score across left ventricular global longitudinal strain (LV GLS) groups in patients with left anterior descending (LAD) artery stenosis 30–50%

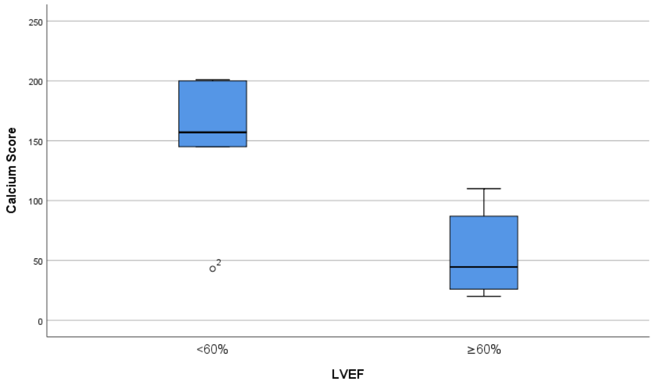

Figure 2. Distribution of calcium score across left ventricular ejection fraction (LVEF) groups in patients with left anterior descending (LAD) artery stenosis 30–50%

No statistically significant differences in LVEF or GLS in relation to CAC score were observed among patients with RCA or Cx stenosis, or in those with three-vessel disease (30-50%).

DISCUSSION

This study demonstrated that hypertensive patients with mild to moderate LAD stenosis (30–50%) and negative treadmill stress tests may exhibit subclinical systolic LV dysfunction, despite the absence of hemodynamically significant coronary obstruction. A significant association was found between higher CAC scores and impaired LV function, expressed as decreased GLS and lower LVEF, in patients with LAD stenosis (30–50%). No such relationship was observed for RCA or Cx stenosis, suggesting that calcific atherosclerotic burden within the LAD may contribute more directly to early myocardial dysfunction than similar lesions in other coronary branches (14–16).

While treadmill stress testing is commonly used to detect ischemia, its diagnostic sensitivity is limited, particularly for non-obstructive or single-vessel disease, which may not produce sufficient perfusion deficits to be detected by functional testing (2–4). These findings underscore the clinical importance of CAC scoring in this patient population. A higher CAC score likely reflects both calcified atherosclerotic plaque and a higher burden of subclinical microvascular and endothelial dysfunction, which can compromise myocardial perfusion and contribute to subendocardial ischemia (17,18).

Given the LAD's central contribution to longitudinal fibre shortening and overall LV contractility, this finding is physiologically plausible (16,19,20). Even mild LAD stenosis accompanied by elevated CAC could represent an early stage of structural–functional uncoupling between coronary anatomy and ventricular mechanics.

Beyond coronary anatomy, chronic systemic inflammation may contribute to myocardial dysfunction through endothelial dysfunction, microvascular impairment, and myocardial fibrosis, thereby promoting LV systolic dysfunction (21–24). These mechanisms may partly contribute to the observed association. In addition, long-standing hypertension with volume overload and concentric remodelling may adversely affect longitudinal fibre performance and contribute to early myocardial dysfunction (25–27).

From a clinical perspective, the combined use of CAC scoring and STE may enable risk stratification beyond conventional testing by identifying patients with subclinical LV dysfunction and an increased risk of adverse remodeling (9,28,29). These findings highlight limitations of relying solely on anatomical assessment, as patients undergoing CCTA may be considered "normal" in the absence of significant stenosis despite persistent symptoms (30,31). Symptomatic patients may require functional assessment beyond anatomical imaging alone, with consideration of advanced techniques such as CT-derived fractional flow reserve (CT-FFR), alongside closer clinical surveillance and strict cardiovascular risk factor control (32–36).

It is important to consider the limitations of CCTA, including radiation exposure (37). Although CCTA offers a non-invasive and rapid anatomical assessment, its diagnostic sensitivity (92–95%) and specificity (approximately 60–65%) remain imperfect, particularly in differentiating mild to moderate stenoses or in heavily calcified segments where blooming artifacts can obscure evaluation (32,38). CCTA should not be used as the sole determinant of "normal" coronary status, especially in symptomatic patients or those with elevated CAC scores, where functional impairment or microvascular disease may exist (39) .

This study is limited by its relatively small sample size and cross-sectional design, precluding causal conclusions. Moreover, perfusion imaging or invasive physiological measurements were not performed. Despite strict exclusion criteria, residual confounding cannot be excluded.

To our knowledge, this is the first study to demonstrate a territory-specific association between LAD-related coronary calcific burden and subclinical LV systolic dysfunction in hypertensive patients with mild LAD stenosis and negative exercise testing. By integrating anatomical (CCTA/CAC) and deformation imaging (GLS), our findings extend existing evidence to the early phase of LAD disease and support closer clinical surveillance in this population.

In conclusion, higher CAC scores in hypertensive patients with mild LAD stenosis and negative stress testing identify those at risk of subclinical LV dysfunction. Conventional functional testing alone may underestimate myocardial impairment in patients with non-significant LAD disease. The combined use of CAC scoring and STE could therefore provide a more sensitive, non-invasive approach for detecting early systolic dysfunction and identifying patients at higher cardiovascular risk. Future prospective studies with larger cohorts are warranted to clarify the prognostic implications of early subclinical LV dysfunction in this population.

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CONFLICTS OF INTEREST

None to declare.

ETHICS STATEMENT

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional

Ethics Committee of the General Hospital “Prim. dr. Abdulah Nakas”.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request and with permission of the institution.

AUTHOR CONTRIBUTIONS (CRediT)

Conceptualization: E.B., N.M.-V.; **Data curation:** A.D., N.M.-V., E.N.; **Investigation:** A.D., N.M.-V., E.N.; **Methodology:** E.B., N.M.-V., A.M., B.S.; **Supervision:** E.B., A.M., T.K.-P., M.O.; **Writing – original draft:** N.M.-V.; **Writing – review & editing:** E.B., A.D., N.M.-V., E.N., A.M., B.S., T.K.-P., M.O. All authors have read and agreed to the published version of the manuscript.

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