Case Report
The zero calcium score paradox and multivessel obstructive disease: a case report of a patient with zero CAC score

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Abstract: A coronary artery calcium (CAC) score of 0 is generally indicative of a low risk for both all-cause mortality and cardiovascular events, often serving as a basis for excluding obstructive coronary artery disease (CAD). Although isolated cases of coronary involvement have been reported in patients with a CAC score of 0, the incidence of extensive multivessel disease under these circumstances is exceedingly rare. A 48-year-old man with diabetes and hypercholesterolemia presented with atypical non-exertional left-sided chest pain. Despite a nonspecific ECG, a HEART score of 3, and a zero CAC score on echocardiography, coronary computed tomography angiography (CCTA) revealed multiple non-calcified plaques in the right coronary artery (RCA), right posterior descending coronary artery (RPDA), and left circumflex artery (LCX). The patient underwent staged percutaneous coronary intervention with drug-eluting stents, resulting in complete resolution of the stenosis. At the one-month follow-up, he remained symptom-free and tolerated the medication regimen well. This case report demonstrates that a zero CAC score should not preclude further evaluation in high-risk symptomatic patients. Extensive non-calcified plaques causing significant luminal obstruction underscore the limitations of CAC scoring, highlighting the need for additional imaging modalities, such as CCTA, to achieve timely and accurate diagnoses and appropriate therapeutic interventions.

Keywords: Coronary artery calcium, coronary artery disease, coronary computed tomographic angiography

Introduction

Coronary artery disease (CAD) is characterized by the progressive buildup of atherosclerotic plaques within the coronary arteries, ultimately resulting in luminal narrowing or complete occlusion. Early risk assessment and detection are critical for the effective management and prevention of adverse cardiac events [1, 2]. Coronary computed tomography angiography (CCTA) has emerged as the premier noninvasive technique for evaluating both calcified and non-calcified atherosclerotic plaques, as well as for assessing the extent of coronary luminal stenosis [3].

The coronary artery calcium (CAC) scoring method is a noninvasive imaging procedure used to quantify the burden of calcified athero-sclerotic plaques in the coronary arteries. This method uses non-contrast cardiac computed tomography (CT) scans to detect and quantify calcium deposits in the walls of the coronary arteries. Each calcified lesion was scanned based on its surface area and peak density, which were summed across all coronary arteries to yield the total CAC score. The resulting score was then used to stratify patients into various risk categories, from no detectable calcification (0 score) to extensive calcification (high scores), which is associated with a high risk of CAD and poor cardiac events [4]. The prevalence and severity of coronary calcification, as indicated by the CAC score, serve as indirect markers of the total atherosclerotic plaque burden, thereby increasing the risk of myocardial infarction and other cardiovascular events. Although the CAC score does not
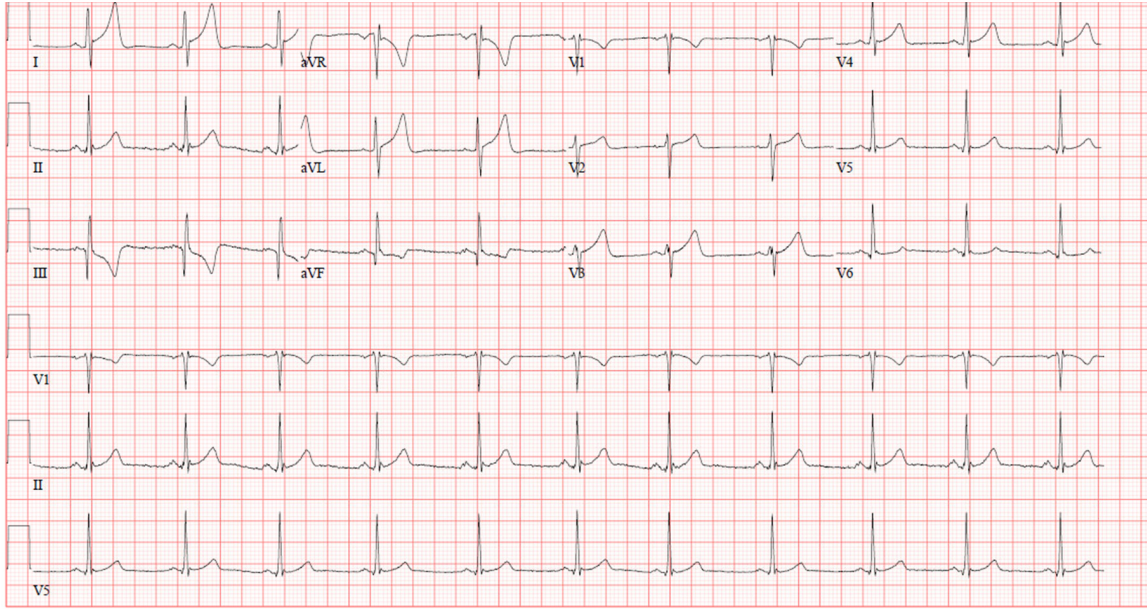
Figure 1. The EKG of our case. The EKG demonstrates nonspecific ST-segment and T-wave changes, which, despite being inconclusive, prompted further cardiac evaluation due to the patient's significant cardiovascular risk factors.

directly assess cardiac function, it has been associated with subclinical alterations in cardiac function, specifically left ventricular diastolic dysfunction (LVDD) [5].

A CAC score of 0 is generally indicative of a low risk of both all-cause mortality and cardiovascular events, often serving as the basis for excluding obstructive CAD [4]. However, the predictive reliability of the CAC score may be diminished in symptomatic patients, especially those presenting with significant cardiovascular risk factors [6]. Although isolated cases of coronary involvement have been reported in patients with CAC scores of 0 [7], the incidence of extensive multivessel disease in these cases is exceedingly rare. This case report details a patient exhibiting generalized coronary involvement despite a CAC score of 0, underscoring the need for an integrated imaging strategy for comprehensive risk evaluation in asymptomatic patients.

Case presentation

A 48-year-old man with a known history of diabetes mellitus and hypercholesterolemia presented to our hospital with a chief complaint of atypical chest pain. He described the pain as a stabbing sensation localized to the left chest, unassociated with exertion and without radia-tion. Although his chest pain did not exhibit the classical features of angina, the presence of significant cardiovascular risk factors necessitated further evaluation.

At the initial assessment, his vital signs were as follows: heart rate, 70 beats/min; blood pressure, 110/78 mmHg; respiratory rate, 18 breaths/min; and oxygen saturation (SpO2), 96% on room air. Physical examination findings were unremarkable. Electrocardiography (ECG) demonstrated nonspecific ST-segment and T-wave changes (**Figure 1**). The patient's HEART score (History, ECG, Age, Risk factors, and troponin) was 3, based on nonspecific ECG changes, the presence of two risk factors, and age.

Despite the low HEART score, additional work-up is required. The patient underwent trans-thoracic echocardiography and coronary computed tomography angiography (CCTA). Echocardiography revealed preserved global left ventricular systolic function with possible regional wall motion abnormalities. The mean coronary artery calcium (CAC) score was zero. However, CCTA revealed multiple non-calcified plaques in the right coronary artery (RCA), right posterior descending coronary artery (RPDA), and left circumflex artery (LCX) (**Figure 2**). To confirm these findings, invasive coronary angi-
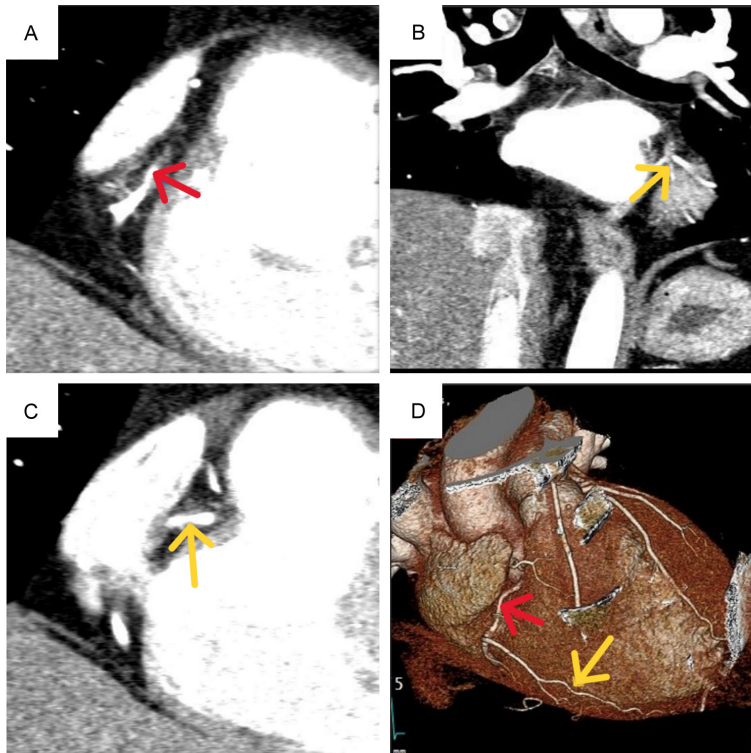
Figure 2. A. Distal right coronary artery (RCA) with a non-calcified plaque causing significant stenosis. B. Left circumflex artery (LCX) showing a non-calcified plaque with moderate stenosis. C. Proximal RCA with a large non-calcified plaque resulting in severe stenosis. D. 3-dimensional volume rendering highlighting the stenosis in the proximal RCA (red arrow) and distal RCA (yellow arrow).

ography was performed, which revealed severe stenosis in the proximal and mid-to-distal segments of the RCA, as well as significant lesions in the posterolateral artery (PLA) and second obtuse marginal (OM2) branch (**Figure 3**).

Interventional management was initiated with percutaneous coronary intervention (PCI) for the proximal and distal RCA lesions. Three days later, a subsequent PCI was performed, targeting the PLA and OM2. Successful deployment of drug-eluting stents resulted in complete resolution of the stenosis, and the procedure was completed without complications (**Figure 3**). Post-procedure, the patient was started on dual antiplatelet therapy (aspirin and clopidogrel), and further management was instituted to address his dyslipidemia.

At the one-month follow-up, the patient remained symptom-free and demonstrated excellent tolerance to the medication regimen.

Discussion

This case highlights the diagnostic challenges and clinical implications of a zero CAC score in symptomatic CAD. Our patient, a 48-year-old man with significant metabolic risk factors, presented with atypical chest pain and an initially reassuring CAC score of 0. Nonetheless, CCTA revealed an extensive non-calcified plaque burden involving three major coronary territories (RCA, RPDA, and LCX), which was subsequently confirmed by invasive coronary angiography.

The use of the CAC score for risk stratification is a long-established method that has proven effective in elderly populations. Extensive epidemiological studies indicate that among individuals with predominantly calcified plaques, commonly observed in older patients, a zero CAC score serves as a robust indicator of low risk [4]. Sheppard et al. [8], have demonstrated that a zero CAC reading correlates with extremely low annual event rates and a high negative predictive value for excluding obstructive CAD in older individuals. However, the utility of the CAC score as a diagnostic tool may vary considerably when applied to younger populations or patients with early stage atherosclerosis [9, 10]. Furthermore, Agha et al. [11] conducted a meta-analysis of over 92,000 patients who experienced either stable or acute chest pain. Their findings indicated that the absence of CAC was correlated with a very low prevalence of obstructive CAD, a low prevalence of nonobstructive CAD, and a low annualized risk of major adverse cardiac events. Consequently, these results endorse the utility of a CAC score of zero within a value-based healthcare delivery model, serving as an effective gatekeeper for more advanced imaging in patients presenting with chest pain. In our case, although the patient was in his late forties, his significant risk factors, such as diabe-
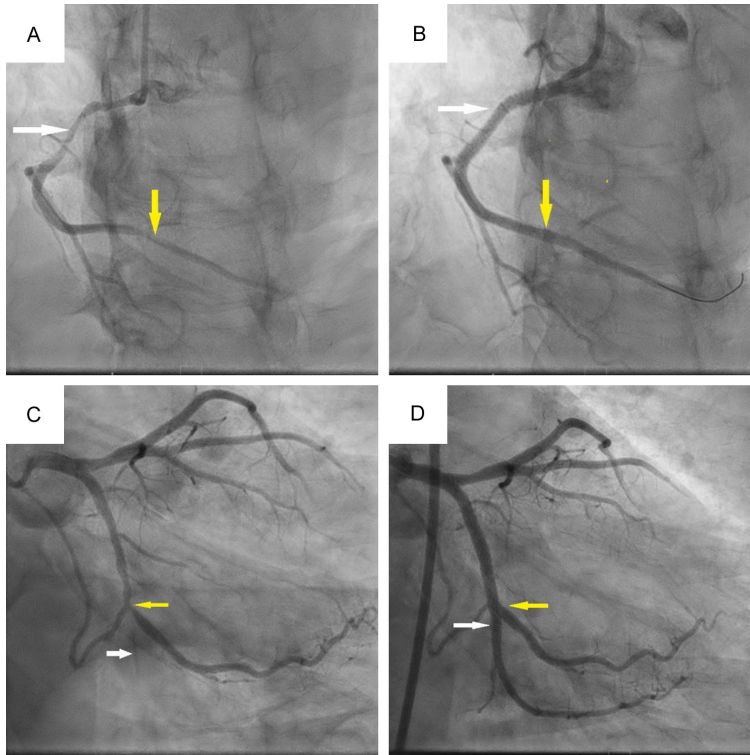
Figure 3. A. Pre-percutaneous coronary intervention (PCI) image demonstrating severe stenosis in the proximal and distal segments of the right coronary artery (RCA). B. Post-PCI image of the RCA following deployment of a drug-eluting stent, showing complete resolution of the stenosis. C. Pre-PCI image revealing significant lesions in the posterolateral artery (PLA) (white arrow) and the second obtuse marginal (OM2) branch (yellow arrow). D. Post-PCI image of the PLA (white arrow) and OM2 (yellow arrow) after successful stent placement, with restored luminal patency.

tes and hypercholesterolemia, likely accelerated the development of non-calcified plaques.

Despite a zero CAC score generally indicating low cardiovascular risk, our case demonstrates that comprehensive evaluation remains essential for patients with significant risk factors. For suspected CAD, diagnostic approaches should be individualized based on risk profile regardless of CAC findings. In younger patients with metabolic disorders like diabetes and hypercholesterolemia, non-calcified plaques often predominate in early disease stages, potentially escaping detection through calcium scoring alone.

Traditionally, calcification is considered a marker of late-stage plaque development. In the early natural history of atherosclerosis, especially when metabolic dysfunction such as uncontrolled diabetes or hypercholesterolemia is present, plaques are often non-calcified.

Therefore, relying solely on CAC scores for risk evaluation might lead clinicians to underestimate the overall plaque burden in high-risk individuals [12]. Despite a zero CAC score generally indicating low cardiovascular risk, our case demonstrates that comprehensive evaluation remains essential for patients with significant risk factors. For suspected CAD, diagnostic approaches should be individualized based on risk profile regardless of CAC findings. In younger patients with metabolic disorders like diabetes and hypercholesterolemia, non-calcified plaques often predominate in early disease stages, potentially escaping detection through calcium scoring alone. This observation highlights the need for additional imaging techniques, such as CCTA, which allows the visualization of both calcified and non-calcified lesions.

CCTA plays a crucial role in identifying non-calcified plaques that would be missed if evaluation stopped after zero CAC scoring. This multimodality imaging approach is particularly important for high-risk patients with concerning symptoms. When CCTA identifies significant stenosis, invasive coronary angiography provides definitive confirmation and intervention opportunities.

Also, a score of zero for CAC does not rule out the existence of severe stenosis of the coronary arteries because non-calcified plaques may also produce obstruction and manifest with ischemic events. In these patients, management should extend beyond dual antiplatelet therapy to prevent stent thrombosis. Statins are indicated or need to be continued despite a zero CAC score, especially in the presence of elevated levels of low-density lipoprotein (LDL) cholesterol, as statins stabilize plaque and hinder atherosclerosis. In addition to pharmacological treatment, vigorous modification of cardiovascular risk factors, such as control of

hypertension and diabetes, cessation of smoking, maintenance of body weight, and encouragement of a health-promoting lifestyle, is required to reduce the overall risk [13, 14]. In the presence of severe or symptomatic coronary stenosis, revascularization via PCI or coronary artery bypass grafting (CABG) is to be considered. The decision to perform revascularization hinges on the severity and complexity of the lesions, patient symptoms, and global risk profile, with a frequent need for a multidisciplinary Heart Team [15]. Antithrombotic therapy, aside from initial dual antiplatelet therapy, in long-term management, must be individualized according to the patient's thrombotic and bleeding risks, with possible single antiplatelet therapy or oral anticoagulation, if warranted by other comorbidities, such as atrial fibrillation.

Importantly, our patient demonstrated an unusual degree of disease severity. While most studies report the presence of blockages in one or two coronary vessels in patients with a CAC score of zero [16, 17], our case was notable for significant stenosis in three major coronary arteries. This finding not only reinforces the limitations associated with the "power of zero" but also emphasizes that multivessel obstructive disease can occur even when traditional imaging findings are reassuring. The integration of CCTA with invasive coronary angiography in this case provided a complete anatomical assessment, enabling targeted PCI, which led to an excellent outcome.

The role of integrated imaging in such scenarios is significant. Patients diagnosed with metabolic disorders who experience chest pain should be concerned about the CAC score limitations before accepting a zero-score result. Whereas CAC scoring offers rapid risk stratification for asymptomatic patients, CCTA provides critical complementary anatomical details, particularly in symptomatic patients with high cardiovascular risk profiles [3]. In our patient, the detection of extensive non-calcified plaques underscored the importance of not being reassured solely by a zero CAC, as the negative predictive value of CAC scoring appears to be less robust in the presence of early atherosclerotic changes. Moreover, the three-vessel involvement seen here contrasts with reports from other cohorts, where only one or two vessel blockages were documented, thereby alerting clinicians to the possibility

of more widespread disease in select high-risk individuals.

In summary, the combination of clinical evaluation with risk factor analysis and multiple imaging modalities delivers the most thorough diagnostic and therapeutic solution for managing CAD in younger patients with metabolic dysfunction and may receive misleading zero CAC scores. The presented case demonstrates the variable nature of coronary atherosclerosis because early non-calcified plaques can produce substantial blockages even before calcium deposits form, thus requiring ongoing screening in populations at high risk, regardless of their CAC results.

Conclusion

In summary, this case report demonstrates that a zero calcium score should not automatically lead to the exclusion of further diagnostic workup in symptomatic patients. Identifying extensive non-calcified plaques across three coronary territories, rather than the commonly reported one or two vessels, reinforces the limitations of CAC-based risk assessment, particularly in younger or high-risk patients with metabolic derangements. Advanced imaging modalities, including CCTA and invasive angiography, remain indispensable tools for thorough evaluation and timely therapeutic intervention in such cases.

Disclosure of conflict of interest

None.

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