JACC: CASE REPORTS VOL. 29, 2024

© 2024 THE AUTHORS. PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN
COLLEGE OF CARDIOLOGY FOUNDATION. THIS IS AN OPEN ACCESS ARTICLE UNDER
THE CC BY-NC-ND LICENSE (http://creativecommons.org/licenses/by-nc-nd/4.0/).

#### **CORONARY ARTERY DISEASE**

**IMAGING VIGNETTE: CLINICAL VIGNETTE** 

# The Zero Calcium Score Paradox



Rachad Ghazal, MD, a Danish Bawa, MD, Adnan Ahmed, MD, Dhanunjaya Lakkireddy, MD, Vasvi Singh, MD

### **ABSTRACT**

Our study presents a case of angina with a zero calcium score yet severe coronary stenosis from noncalcified plaque. We highlight the limitation of otherwise prognostically powerful coronary calcium score as a singular predictive tool especially when used in symptomatic patients. (J Am Coll Cardiol Case Rep 2024;29:102233) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

oronary artery disease (CAD) remains a significant health concern, and coronary artery calcium (CAC) scoring is a powerful tool for risk stratification, primarily in asymptomatic individuals. Notably, a CAC score of 0 often indicates a low risk for CAD and major adverse cardiac events and an excellent long-term prognosis. However, its diagnostic accuracy in symptomatic patients remains debated.

A 56-year-old man with hypertriglyceridemia managed with lifestyle modification presented to the cardiology clinic for evaluation of angina. Vital signs revealed a heart rate of 58 beats/min, blood pressure of 138/90 mm Hg, with normal respiratory rate, and normal respiratory rate, and saturation of peripheral oxygen (SpO<sub>2</sub>). Physical examination was unremarkable. Electrocardiography demonstrated sinus bradycardia with nonspecific ST-segment changes (Supplemental Figure 1). The patient's atherosclerotic cardiovascular disease risk score was calculated to be 9.2%, indicating intermediate 10-year risk. Transthoracic echocardiogram and coronary computed tomography angiography (CCTA) were ordered for further evaluation. Transthoracic echocardiogram revealed a left ventricular ejection fraction of 60%-65% and normal ventricular and diastolic functions. CCTA CAC score was 0. However, a significant noncalcified plaque was observed in the distal right coronary artery (RCA), causing severe stenosis (70%-99%) (Figures 1A to 1C). Fractional flow reserve via computed tomography distal to the RCA lesion was found to be hemodynamically significant at 0.50 (Figure 1D).

The patient underwent invasive coronary angiography for percutaneous coronary intervention on the distal RCA lesion. Invasive coronary angiography confirmed the severe stenosis in the distal RCA as initially seen on CCTA. The patient was successfully treated with a drug-eluting stent, leading to the complete resolution of the distal RCA stenosis without any associated complications (Figures 1E and 1F). Postprocedural assessment indicated resolution of the anginal symptoms. The patient was initiated on dual antiplatelet therapy, hypertension control, and lipid control. At the 1-month follow-up, the patient remained asymptomatic, tolerated his medications well, and had normal blood pressure.

From the <sup>a</sup>Kansas City Heart Rhythm Institute and Research Foundation, Overland Park, Kansas, USA; and the <sup>b</sup>Midwest Heart and Vascular Specialists, HCA Midwest Health, Overland Park, Kansas, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received October 9, 2023; revised manuscript received January 4, 2024, accepted January 8, 2024.

# ABBREVIATIONS AND ACRONYMS

CAC = coronary artery calcium

CAD = coronary artery disease

**CCTA** = coronary computed tomography angiography

RCA = right coronary artery

### **DISCUSSION**

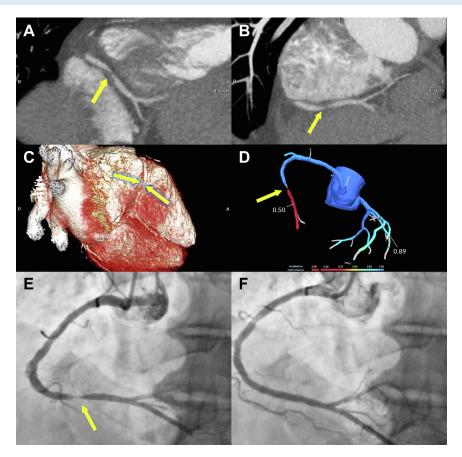
Whereas CAC scoring effectively detects CAD in asymptomatic individuals due to its high sensitivity and negative predictive value, its specificity and positive predictive value are comparatively limited in symptomatic patients. Therefore, the absence of coronary calcification does not rule out atherosclerotic plaque, because noncalcified plaque is not accounted for in CAC scoring.

In the presented case, the patient had severe stenosis from noncalcified plaque in the RCA despite a zero calcium score from a complete CCTA. This highlights the limitations of using CAC score alone for

CAD detection in symptomatic individuals and adds to the published data on the limitations of the absolute diagnostic power of CAC scoring, especially overlooking noncalcified plaque CAD.

The "zero calcium paradox" raises questions about the true predictive value of a zero calcium score.<sup>2</sup> Although often reassuring, it should not be the sole criterion for ruling out significant CAD. A lack of coronary calcification does not necessarily indicate an absence of atherosclerotic plaque. Although CAC scoring is traditionally used for asymptomatic individuals, its use is increasingly extending to symptomatic populations, necessitating caution in interpretation. The "power of zero" mainly applies to asymptomatic patients, with the exception of younger individuals (<40 years) with cardiovascular risk factors such as diabetes mellitus and hypercholesterolemia.<sup>3</sup>

FIGURE 1 Excellent Correlation Between Coronary Computed Tomography Angiography and Invasive Coronary Angiography in a High-Risk Symptomatic Patient With Noncalcified Plaque Causing Severe Stenosis in the Right Coronary Artery



Coronary computed tomography angiography (A, B), 3-dimensional volume rendering (C), and Fractional flow reserve computed tomography (D) demonstrating noncalcified plaque (yellow arrows) involving a discrete segment of the mid to distal right coronary artery within the posterior right atrioventricular groove, causing severe stenosis (70%-99%). Coronary angiography images showing pre- (E) and post- (F) percutaneous transluminal coronary angioplasty of right main coronary artery along with a drug-eluting stent.

### **FUNDING SUPPORT AND AUTHOR DISCLOSURES**

Dr Singh has received research funding from the American Society of Nuclear Cardiology and Pfizer; and has served on Pfizer's Speakers Bureau and Advisory Committee. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

**ADDRESS FOR CORRESPONDENCE**: Dr Vasvi Singh, Midwest Heart and Vascular Specialists, HCA Midwest Health, 5100 W 110th Street, Suite 200, Overland Park, Kansas 66211, USA. E-mail: vasvi.singh@hcahealthcare.com. @SinghVasvi.

## REFERENCES

- **1.** Nasir K, Cainzos-Achirica M. Role of coronary artery calcium score in the primary prevention of cardiovascular disease. *BMJ*. 2021;373:n776.
- **2.** Mortensen MB, Gaur S, Frimmer A, et al. Association of age with the diagnostic value of coronary artery calcium score for ruling out coronary stenosis in symptomatic patients. *JAMA Cardiol*. 2022;7(1):36-44.
- **3.** Sama C, Abdelhaleem A, Velu D, et al. Non-calcified plaque in asymptomatic patients with zero coronary artery calcium score: a systematic review and meta-analysis. *J Cardiovasc Comput Tomogr.* Published online October 9, 2023. https://doi.org/10.1016/j.jcct.2023.10.002

KEY WORDS arterial plaque, coronary artery calcium score, coronary artery disease, coronary atherosclerosis, coronary calcification, CTA coronary angiography

**APPENDIX** For a supplemental figure, please see the online version of this paper.