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Short Report

Coronary artery calcium in a 20-year-old South Asian patient - pushing the limits of detecting "early disease"

Erfan Tasdighi [a], Charlie Brumley [b], Aashna Vajramani [b], Michael J Blaha [a], Anandita Agarwala [b,*]

[a] Johns Hopkins University, Baltimore, MD, United States
[b] Center for Cardiovascular Disease Prevention, Cardiovascular Division, Baylor Scott and White Health Heart Hospital Baylor Plano, Plano, TX, United States

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ABSTRACT

Coronary artery calcium (CAC) assessment has long been reserved for intermediate-risk individuals in mid- to older-adult populations. However, a growing body of evidence supports expanding CAC measurement to younger adults who exhibit multiple risk factors or other risk-enhancing features. We describe a case of a very young, 20-year-old, South Asian man with a CAC score of 15.7 Agatston Units. Despite his age and lack of overt symptoms, his CAC score placed him at the 99th percentile for his age and sex, underscoring the limitations of relying solely on traditional risk algorithms. Early CAC detection in such patients has potential for significant clinical impact, allowing timely implementation of intensive lifestyle modification and the most aggressive possible pharmacotherapy for cardiovascular risk reduction.

Evidence indicates that even minimal CAC in very young individuals can progress exponentially, markedly increasing the risk of future atherosclerotic cardiovascular disease. Nonetheless, current guidelines do not recommend CAC testing in this population, creating a missed opportunity to detect and intervene in high-risk individuals during early adulthood. These observations underscore the need for more precise risk stratification strategies in select high-risk populations. Incorporating CAC measurements into care for young, high-risk individuals—alongside newer tools such as polygenic risk scores and low-radiation coronary CT angiography—could revolutionize preventive cardiology. Further research is needed to refine the cost-effectiveness and implementation strategies for early CAC measurement, develop more inclusive guidelines, and ensure a specialized workforce capable of delivering comprehensive preventive care.

1. Learning objectives

To emphasize the importance of preventive testing for those with a family history of premature cardiovascular disease

To recognize the potential utility of selective CAC testing among select very low-risk young patients with risk enhancing factors

2. Background

Coronary artery calcium (CAC) screening has been traditionally recommended for intermediate-risk patients, for example, according to the 2018 American Heart Association (AHA)/American College of Cardiology (ACC)/Multi-society cholesterol guideline or the 2019 AHA/ACC Prevention guideline [1,2]. However, emerging applications in lower-risk patients with risk-enhancing factors are becoming increasingly discussed, including among younger individuals (i.e., those below 40 years old) who are traditionally not considered for CAC screening. We present a unique and illustrative case of a 20-year-old patient with a CAC score of 15.7 Agatston Units.

3. History of presentation

An asymptomatic 20-year-old South Asian man who was born in India and immigrated to the U.S. 2 years prior to his initial presentation presented for a preventive cardiovascular evaluation due to a high-risk family history. He has no past medical history and does not take any medications. He is able to exert himself to the extent that he desires without any cardiovascular symptoms or limitations. He is a college

* Corresponding author.
E-mail address: anandita.kulkarni@bswhealth.org (A. Agarwala).

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student with a family history of premature cardiovascular disease in his mother, who had a myocardial infarction (MI) and coronary artery bypass surgery in her 40s. He engages in moderate physical activity and consumes a standard Western college student dietary pattern. He has no history of smoking and no alcohol or illicit drug use. His office-based vital signs were as follows: blood pressure 137/86 mmHg (with home blood pressure reading of 120–125/75–80 mmHg), heart rate of 93 bpm, weight of 98.6 kg, height of 170.2 cm, and BMI of 34.0 kg/m^2. His physical examination was unremarkable outside of increased abdominal adiposity with no sign of increased cholesterol including xanthelasma and insulin resistance such as acanthosis nigricans. His recent laboratory work showed a hemoglobin A1c level of 5.5 %, total cholesterol of 129 mg/dL, high-density lipoprotein cholesterol (HDL-C) of 41 mg/dL, low-density lipoprotein cholesterol (LDL-C) of 61 mg/dL, and triglycerides of 135 mg/dL. Lipoprotein(a) was below 20 mg/dL. His primary goal at this initial visit was risk assessment, given the family history of premature CAD in his mother.

4. Decision-Making

In our assessment, our attention shifted to atherosclerosis imaging given the uncertain role of polygenic risk score (PRS) testing in his age group and in his race/ethnicity. We deliberated the indications and potential limitations of CAC testing for an individual of his age. The patient was counseled in advance that a CAC score of zero would not be as actionable in his age group and that aggressive lifestyle-based and potentially pharmacologic preventive measures would still be undertaken. A primary constraint was that fewer than 5 % of unselected individuals from a general clinical population in a similar age range present with a CAC score exceeding zero [3]. However, given his family history of premature coronary artery disease—particularly in his mother—his South Asian ancestry, and his cardiometabolic risk factors, the mutual decision was made to proceed with CAC scoring. Moreover, a previous study demonstrated the non-negligible prevalence of CAC among very high-risk 20–30 years old US adults by showing that individuals with ≥3 traditional risk factors had a statistically significant higher odds of having prevalent CAC (OR 5.57, 95 % CI; 1.82–17.03) compared to participants with no risk factors [4].

His total CAC score amounted to 15.7 Agatston Units (AU), comprising 6.82 AU in the right coronary artery and 7.91 AU in the left circumflex (Fig. 1). This would be expected to place him in the 99th percentile for his age and sex group, extrapolating from (the www.cac-tools.com tool). Moreover, considering the anticipated progression of CAC score by about 20 %- 25 % annually (i.e. reflecting exponential growth), even a very low CAC score early in life can reach a very high CAC score in early adulthood. For example, this patient would be expected to reach CAC score of 100 in ~10 years (age 30), 300 in 16 years (age 36), and 1000 when he is approximately 43 years old [5].

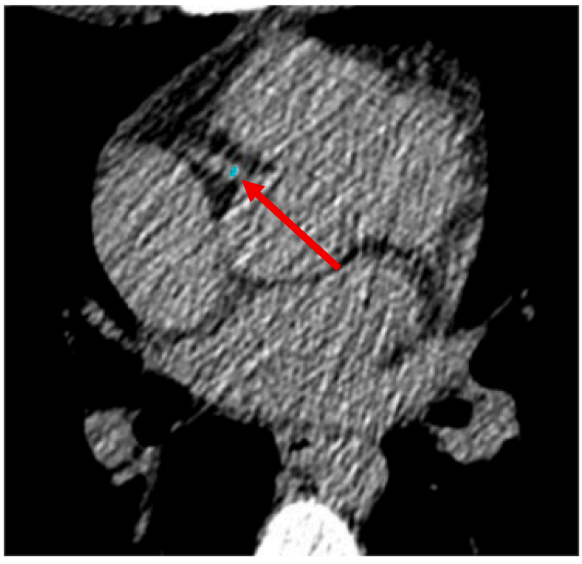

Fig. 1. CT Image from Patient's Coronary Artery Calcium Screening
The red arrow pointing to the blue coloring highlights the plaque found in the patient's right coronary artery amounting to a score of 6.82 AU.

On his subsequent visit, we showed him his CAC scan results to solidify the individual nature of his risk assessment, and we explained their interpretation in context with the assistance of www.cac-tools.com and other websites. He initiated high-intensity combination lipid-lowering therapy with rosuvastatin 20 mg daily and ezetimibe 10 mg daily, anticipating an up to 70 % LDL-C reduction. Moreover, intensive lifestyle interventions were recommended in accordance with current guideline recommendations. He met with a dietitian and received counseling on the DASH and Mediterranean diet as well as the means to modify meals traditionally found in South Asian diet. He was also counseled on guideline recommendations for physical activity to help assist with weight loss with at least five days per week with moderate intensity and 30 min of duration consistent of both aerobic and resistance training [6].

It is important to note that, upon reviewing his objective data—including the CAC score and its potential progression—the patient was strongly encouraged to adhere to preventive measures, ultimately prompting him to make significant lifestyle changes. Unfortunately, he relocated abroad, making in-person follow-up visits unfeasible. Nevertheless, he was advised to maintain regular clinical evaluations in his home country to monitor and manage his cardiovascular risk.

5. Discussion

South Asians face a heightened risk of atherosclerotic cardiovascular disease (ASCVD) and exhibit a greater mortality rate from ASCVD compared to most other racial/ethnic groups [7]. An AHA Scientific Statement highlighted that most of the risk for ASCVD among South Asians living in the US (SAUS) can be attributed to traditional ASCVD risk factors [8]. To improve prevention efforts among SAUS, the 2018 AHA/ACC/Multi-society guideline on the management of blood cholesterol [1] and the 2019 ACC/AHA primary prevention guideline [2] list South Asian ethnicity as a "risk-enhancing factor" to guide ASCVD risk stratification.

CAC is a focal point of research, clinical practice, and international guidelines for early detection of subclinical coronary artery disease and allocating preventive therapies [9,10]. The emphasis on CAC is due to its simplicity, wide accessibility, and strong improvement in ASCVD risk prediction beyond traditional risk factors [11]. Using risk stratification tools like the CAC score could help individualize the allocation of preventive interventions. Previous studies among SAUS adults showed that South Asian men had greater CAC progression than Chinese, Black, and Latino men but similar progression to that of Whites after adjusting for traditional risk factors [12].

CAC scoring in very young individuals (i.e., age < 30 years old) has several potential limitations. A zero CAC score does not 100 % rule out the presence of atherosclerosis or the future long-term development of cardiovascular disease, as young individuals may still have minimal early non-calcified plaques that the test cannot detect. Used incorrectly, this can lead to a false sense of security and delay in patient follow-up or initiating preventive therapies in those with significant risk factors. Moreover, the "warranty period" for a zero CAC score, which is the duration within which the score reliably indicates no plaque or low risk, is less certain for younger adults. In select very young patients with emerging poor lifestyle traits, their risk factors may evolve more rapidly, necessitating more frequent re-assessments compared to older populations. The commonly used CAC score calculator for young individuals is only for adults aged 30 to 45 years and does not account for individuals younger than 30 or racial and ethnic groups beyond African

American and White populations [13].

It can be argued as an alternative approach that when encountering a very young patient with increased traditional risk factors we can start the lifestyle modification and even low dose statin therapy to mitigate the cardiovascular risk without measuring the CAC score [14]. However, if the presence of a CAC in a very young patient was not found we might have missed the opportunity to start the aggressive primary prevention, including statin therapy, blood pressure control, and intensive lifestyle modification[15]. Moreover, CAC may be a helpful tool for motivating patients to initiate and adhere to prevention medications and healthy lifestyle interventions.

The presence of CAC in very young individuals is a highly significant finding with the potential to profoundly change clinical management and long-term risk trajectory. It warrants the most aggressive possible preventive measures which can be expected to save the most quality-adjusted life years compared to an older population. Moreover, recent studies have demonstrated a non-negligible prevalence (3.9 % −13.9 %) of CAC in healthy young adults and its strong association with ASCVD, suggesting its potential to reclassify risk and improve the selection of 30-45 years old individuals who are most likely to benefit from early preventive therapies [16]. Additionally, current guidelines including PREVENT and PCE are not applicable to predict the risk in very young individuals. Therefore, while routine CAC screening is not recommended for all young individuals, it may be considered for those with a very high lifetime risk of ASCVD to better tailor risk management strategies [17].

Detecting CAC in young patients provides critical insights into their long-term cardiovascular risk. The exponential growth of CAC underscores its critical role in cardiovascular risk assessment, especially when detected in young individuals. Identifying CAC $>$ 0 at a younger age provides an opportunity to anticipate future risk and intensify preventive strategies before substantial calcification and associated events occur. As predictive tools become more accurate, their integration into clinical practice can improve outcomes by guiding earlier, more personalized interventions [18]. While guidelines do not currently support routine CAC imaging in this population, leveraging existing chest CT data offers a valuable opportunity for opportunistic screening. This approach not only enhances risk stratification but also supports the early initiation of preventive measures, potentially improving adherence to therapies and long-term outcomes. However, it is important to note that the accuracy for detecting very low CAC scores characteristic of this age group is diminished with non-gated chest CT practice [19].

Integrating the CAC staging system into clinical practice offers a straightforward and practical method for assessing cardiovascular risk. This system classifies patients into stages 0 through 4 based on their absolute CAC scores and age- and sex-adjusted percentiles. Notably, very young individuals with any detectable CAC (i.e., a score greater than zero) are automatically placed above the 90th percentile [20], corresponding to stage 2[21]. For these individuals, it is recommended to initiate lipid-lowering therapy aiming for an LDL-C goal of $<$70 mg/dL. Additionally, low-dose aspirin may be considered for individuals whose absolute CAC score approaches 100 [22].

An important goal for recognizing high-risk patients when they are young is to start intensive lifestyle modifications as early as possible. A systematic review and meta-analysis assessing the effect of diet and/or physical activity interventions in adult South Asians at risk for CVD, showed that combined diet and physical activity interventions significantly lowered blood pressure metrics, BMI, weight, waist circumference, and fasting plasma glucose [23]. Moreover, in a secondary analysis of the Look AHEAD trial, it was shown that intensive lifestyle modification might help in lowering the risk of cardiovascular events when the lower body weight is maintained after weight loss [24]. Given all together, starting intensive lifestyle modification early in life and maintaining a healthy lifestyle for the majority of a lifetime could mitigate cardiovascular outcomes in high-risk individuals.

Besides intensive lifestyle modification, medical management of cardiovascular risk factors is an important aspect of cardiovascular outcomes risk reduction. A scientific statement from the AHA outlines the importance of cardiovascular risk assessment in pediatrics and early management of blood pressure, lipids (LDL-C, TG), blood glucose, activity, diet, weight, and smoking [25]. Moreover, the availability of GLP1-RAs as a successful and sustained therapeutic option for weight management provides the opportunity to mitigate cardiovascular risk [26]. Utilizing GLP1-RAs is estimated to confer the greatest net clinical benefit in individuals with higher CAC scores. Accordingly, over a 5-year period, the number-needed-to-treat for major adverse cardiovascular events (653 vs 79), heart failure (1094 vs 144), chronic kidney disease (1044 vs 144), and all-cause mortality (408 vs 98) differs markedly between those with CAC = 0 and those with CAC $\geq$300. These findings underscore the importance of measuring CAC in younger adults to better guide the allocation of GLP1-RAs for weight management [27].

In the future, CAC score can be integrated with other emerging risk factor indicators including PRS and coronary. For young individuals, PRS can serve as a predictive tool to select candidates for CAC testing, particularly those in the highest genetic risk categories. Research indicates that individuals with high PRS have a significantly elevated lifetime risk of CAD, even when other clinical risk scores suggest low short-term risk. By combining PRS with CAC measurement, clinicians may potentially identify subclinical atherosclerosis early, provide early interventions and supplement PRS and CAC score to traditional risk score to obtain a more precise insight into long-term cardiovascular risk [28]. However, PRS scores have limitations, including reduced generalizability to diverse populations and uncertainties regarding cost-effectiveness [29]. CCTA provides detailed visualization of coronary artery anatomy and allows for the detection of non-calcified plaques, which may go undetected by CAC scoring alone. This is particularly advantageous in younger individuals, where early-stage atherosclerosis may involve predominantly soft plaques. Identifying these plaques could potentially enable timely interventions to prevent the progression of CAD. However, the use of CCTA in very young adults requires careful consideration of factors such as radiation exposure and the impact of identifying more incidental findings in this young population[30]. Moreover, advanced CT technologies, such as third-generation dual-source, dual-energy systems, and high-resolution imaging, can significantly reduce radiation dose (by up to 50 % in some studies) while preserving diagnostic accuracy, thereby making CCTA a more viable option for younger populations in the future [31, 32].

6. Conclusion

CAC increases in a predictable way with age. Thus, it must be recognized that individuals presenting with high scores later in life can potentially be reliably identified years or even decades earlier when they have very low scores. The CAC Percentile Calculator, available at cac-tools.com, which calculates CAC percentiles for individuals aged 30–45, has heightened our awareness of the noteworthy prevalence of CAC in younger populations. Selective use of CAC measurements may be considered in younger patients exhibiting multiple risk factors or risk-enhancing factors.

According to the current guidelines, this patient's first CAC assessment might not have occurred until age 42, at which point his score could easily have exceeded 1000 AU—an event associated with a nearly 1 % prevalence among 42-year-old White men, according to CAC-Tools. By detecting and treating his premature atherosclerosis earlier, we initiated lipid-lowering therapy and lifestyle interventions that have the potential to profoundly alter his disease trajectory. However, his long-term outcomes will largely depend on the continuity and coordination of his care.

This case underscores the crucial role of preventive cardiology at a younger age. Yet, significant questions remain: How do we systematically identify and follow such high-risk individuals? Is there a need for

an ACGME-accredited cardiometabolic fellowship to ensure a pipeline of specialists adept at early detection and intervention? Should we establish more precise guidelines for referring patients to preventive cardiology? A robust, longitudinal strategy, including systematic follow-up and appropriate subspecialty referrals, is a potential option to ensure that high-risk individuals receive the preventive measures needed to prevent or delay their disease progression.

7. Author agreement

This is to certify that all authors have seen and approved the final version of the manuscript being submitted. They warrant that the article is the authors' original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

CRediT authorship contribution statement

Erfan Tasdighi: Writing – review & editing, Writing – original draft, Conceptualization. **Charlie Brumley:** Writing – original draft, Data curation. **Aashna Vajramani:** Writing – original draft, Data curation. **Michael J Blaha:** Writing – review & editing, Conceptualization. **Anandita Agarwala:** Writing – review & editing, Validation, Supervision, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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