CLINICAL VIGNETTE

A Case of Severe Coronary Artery Disease in a Patient with a Coronary Artery Calcium Score of Zero

Christine Sun, MD and Alanna Chau, MD

Case Presentation

A 64-year-old man presented to the emergency department (ED) for worsening chest pain. His past medical history includes pre-diabetes, hyperlipidemia, and episodes of exertional chest pain with prior negative ischemic evaluation. He developed atypical chest pain in 2017, described as burning, sharp pain that was sometimes worsened by exercise and underwent a stress echocardiogram which was negative. In 2019 he developed recurrent exertional chest and neck burning pain. CT coronary calcium scan reported a coronary artery calcium (CAC) score of 0. His chest pain was attributed to non-cardiac etiologies. In a desire to reduce medications, the patient and his primary care doctor used his CAC score to support stopping his statin.

His symptoms were stable until 1 year later when the exertional chest pains character became pressure and tight. His symptoms progressed and he had to stop multiple times during regular activity due to the pain which consistently improved with rest. The day prior to ED presentation, he developed sub-sternal chest pressure, jaw pain, diaphoresis, blurry vision and shortness of breath while taking out the trash with symptoms resolving with rest. He was seen by his primary care physician the next day who referred him to the ED.

In the ED, he was hypertensive, 154/86 mmHg and tachycardic to 90 bpm. His resting electrocardiogram was normal with no ischemic changes and serial troponin tests were also negative. Cardiology was consulted and was concerned for unstable angina. They recommended coronary angiogram for definitive diagnosis and started on dual antiplatelet agents and a high intensity statin. Coronary angiography found severe stenosis of 70-90% in proximal to mid left anterior descending coronary artery. Four drug eluting stents were successfully placed. The patient was discharged on goal directed therapy with aspirin, ticagrelor, atorvastatin, and lisinopril. He underwent cardiac rehabilitation and at 3-month follow up with cardiology had no remaining symptoms.

Discussion

Cardiovascular disease is the leading cause of mortality worldwide with coronary artery disease (CAD) accounting for approximately 50% of such deaths. Thus, the medical community needs to accurately and efficiently screen for CAD. The association between CAD and vascular calcification is well established. Coronary artery calcium scoring was developed to stratify patients at intermediate risk of CAD and measure the extent of atherosclerosis. Because atherosclerosis consists of calcified plaque, the goal of CAC scoring is to measure the degree of coronary calcification radiographically corresponding to the following table:

Degree of coronary artery calcification	Absolute CAC score (Agatston method)	CAC score adjusted for gender, age and ethnicity - percentile	Clinical interpretation
Absent	0	0	Very low risk of future coronary events
Discrete	1-100	≤ 75	Low risk of future coronary events; low probability of myocardial ischemia
Moderate	101-400	76-90	Increased risk of future coronary events (aggravating factor); consider reclassifying the individual as high risk
Accentuated	> 400	> 90	Increased probability of myocardial ischemia

Table 1. Degree of coronary artery calcification by absolute CAC scores and adjusted CAC scores with clinical interpretations.[1]

A CAC score of 0 indicates no coronary calcification on CT and predicts a very low risk of future coronary events with a relative risk of 0.09 (95% CI: 0.04 to 0.20; $p < 0.001$). In a meta-analysis by Sarwar et al., CAC score as a predictor of stenosis greater than 50% has sensitivity of 98%, specificity of 40%, with high negative predictive value (NPV) of 93%, and a positive predictive value (PPV) of 68%.[2] However, the NPV of CAC scoring in symptomatic patients has more variability, with some

studies showing a lower NPV of 66-65%.[3] Since symptomatic high risk lesions often have little or no calcification or calcify late in the atherosclerotic process, they may be missed by CT coronary calcium scans.[3] Min et al. studied progression of a CAC score of 0 to a positive CAC score, with the score increasing by 0.5% in the first year, 1.2% in the second year, 5.7% in the third year, 6.2% in the fourth year, and 11.6% in the fifth year. The mean time to conversion was 4.1 ± 0.9 years.[4] Despite having a CAC score of 0 with a suggested follow up exam in 4-5 years, our patient was confirmed to have significant CAD within 1 year of imaging.

Although CAC scoring can serve as a surrogate for total CAD burden, will not detect noncalcified plaques which we suspect was the case for this patient. Coronary atherosclerotic plaques can be classified as calcified, noncalcified or mixed.[5] Often, noncalcified atherosclerotic plaques are more metabolically active than heavily calcified plaques and are associated with increased risk of acute coronary syndromes. Studies have reported statins changing the microarchitecture of plaques with coronary calcium deposits which potentially increases stability.[6] If the patient had continued his statin therapy instead of stopping, his cardiovascular (CV) event risk could have been lowered. Paradoxically they may also increase degree of coronary artery calcification.[6] Therefore it is important to properly counsel patients on the effects of statins on CAC score and CV event risk to ensure medication compliance.

Conclusion

In conclusion, this case demonstrates that patients with a CAC score of 0 can still have significant CAD. The lower NPV of CAC scoring in symptomatic patients underscores the importance of a detailed history and the selection of the most appropriate test.

REFERENCES

1. **Neves PO, Andrade J, Monção H**. Coronary artery calcium score: current status. *Radiol Bras*. 2017 May-Jun;50(3):182-189. doi: 10.1590/0100-3984.2015.0235. PMID: 28670030; PMCID: PMC5487233.
2. **Sarwar A, Shaw LJ, Shapiro MD, Blankstein R, Hoffmann U, Cury RC, Abbara S, Brady TJ, Budoff MJ, Blumenthal RS, Nasir K**. Diagnostic and prognostic value of absence of coronary artery calcification. *JACC Cardiovasc Imaging*. 2009 Jun;2(6):675-88. doi: 10.1016/j.jcmg.2008.12.031. Erratum in: *JACC Cardiovasc Imaging*. 2010 Oct;3(10):1089. Hoffman, Udo [corrected to Hoffmann, Udo]. PMID: 19520336.
3. **McBride CB, Cheezum MK, Gore RS, Pathirana IN, Slim AM, Villines TC**. Coronary Artery Calcium Testing in Symptomatic Patients: An Issue of Diagnostic Efficiency. *Curr Cardiovasc Imaging Rep*. 2013 Jun;6(3):211-220. doi: 10.1007/s12410-013-9198-0. PMID: 23795234; PMCID: PMC3683145.
4. **Min JK, Lin FY, Gidseg DS, Weinsaft JW, Berman DS, Shaw LJ, Rozanski A, Callister TQ**. Determinants of coronary calcium conversion among patients with a normal coronary calcium scan: what is the "warranty period" for remaining normal? *J Am Coll Cardiol*. 2010 Mar 16;55(11):1110-7. doi: 10.1016/j.jacc.2009.08.088. PMID: 20223365.
5. **Motoyama S, Ito H, Sarai M, Kondo T, Kawai H, Nagahara Y, Harigaya H, Kan S, Anno H, Takahashi H, Naruse H, Ishii J, Hecht H, Shaw LJ, Ozaki Y, Narula J**. Plaque Characterization by Coronary Computed Tomography Angiography and the Likelihood of Acute Coronary Events in Mid-Term Follow-Up. *J Am Coll Cardiol*. 2015 Jul 28;66(4):337-46. doi: 10.1016/j.jacc.2015.05.069. PMID: 26205589.
6. **Xian JZ, Lu M, Fong F, Qiao R, Patel NR, Abeydeera D, Iriana S, Demer LL, Tintut Y**. Statin Effects on Vascular Calcification: Microarchitectural Changes in Aortic Calcium Deposits in Aged Hyperlipidemic Mice. *Arterioscler Thromb Vasc Biol*. 2021 Apr;41(4):e185-e192. doi: 10.1161/ATVBAHA.120.315737. Epub 2021 Jan 21. PMID: 33472400; PMCID: PMC7990692.