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POWER OF ZERO STRONGER THAN “SOFT” PLAQUE

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The authors nicely demonstrate,¹ in a mixed cohort of asymptomatic and symptomatic patients, that the prevalence of non-calcified plaque is not insignificant among those persons with calcium score of zero. Understanding the differences between the symptomatic and asymptomatic cohorts are most important and that wasn't well delineated in the manuscript. Prevalence of disease, significance of non-calcified plaque and pre-test probability are all important factors that vary based on symptomatology. Regardless, there were significant percentages of non-calcified plaque and high risk plaque (8.4%) among those with zero scores. However, major adverse cardiovascular events (MACE) were exceptionally low, reaffirming the 'power of zero' of a calcium score. It has been shown in numerous papers and numerous prospective studies that a zero score confers a very low risk of MACE, which was re-confirmed in this study.² The composite MACE rate for scores of zero was 0.54% over 6.6 years of follow up, resulting in a <0.1%/year event rate. Despite the findings of non-calcified plaque and high risk plaque (both of which have mixed data regarding outcomes, especially in asymptomatic persons), the hard endpoint of MACE was extremely low, calling into question the importance of non-calcified plaque and subsequent cardiovascular events. Pathologic studies suggest that a mixed plaque (one with both components of non-calcified and calcified plaque) are most worrisome,³ so it is possible that this isolated non-calcified plaque is not a major concern, reaffirming the need for calcium scores for risk stratification.

The authors spend a fair amount of time suggesting that ultra-low calcium scores (those <1.0) have higher prevalence of disease than those with scores of zero, yet the MACE event rate for this group was identical to the zero score population (0.6 vs 0.54%, p=0.743). It is unclear if these scores represent actual coronary calcification that were not previously identified, or if these represent areas of increase attenuation due to image noise. Regardless, the low event rate of patients with these features is reassuring. This suggest that one can safely consolidate those patients with ultra-low calcium scores with the zero score, as the primary goal of risk stratification is to identify those persons who are at risk of future ASCVD event, and start appropriate therapies to reduce those events. This paper (with 6.6 year median follow up) strongly reinforces the new 2018 ACC/AHA Cholesterol guidelines⁴ and the 2019 ACC/AHA Prevention guidelines⁵ which suggest that those persons with zero scores do not need statin therapy for 5-10 years.

Given the goal of the CAC score is to risk stratify individuals, and minimal and zero calcified plaque have similar outcomes, there appears no added value to characterizing the minimal non-calcified plaque or high risk plaque in this low risk population.

References:

¹ Senoner T, Plank F, Beyer C, et al. Does coronary calcium score zero reliably rule out coronary artery disease in low-to-intermediate risk patients? A coronary CTA study. *J Cardiovasc Comp Tomo* 2019; doi.org/10.1016/j.jcct.2019.09.009.

² Hecht H, Blaha MJ, Berman DS, Nasir K, Budoff M, Leipsic J, Blankstein R, Narula J, Rumberger J, Shaw LJ. [Clinical indications for coronary artery calcium scoring in asymptomatic patients: Expert consensus statement from the Society of Cardiovascular Computed Tomography.](#) *J Cardiovasc Comput Tomogr* 2017;11(2):157-168. doi: 10.1016/j.jcct.2017.02.010. PMID: 28283309

³ Van den Hoogen IJ, Gianni U, Alawamlh O, et al. What atherosclerosis findings can CT see in sudden coronary death: Plaque rupture versus plaque erosion. *J Cardiovasc Comp Tomo* 2019: in press.

⁴ Grundy, S. M., Stone, N. J., Bailey, A. L., Beam, C., Birtcher, K. K., Blumenthal, R. S., ... Yeboah, J. (2019). 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, 73(24), 3168-3209. <https://doi.org/10.1016/j.jacc.2018.11.002>

⁵ Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019;74:e177-232.