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Editorial

Coronary calcium is all we need for risk assessment, yet we do not use it often enough

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In an investigation published in this issue of *Atherosclerosis*, Zhao et al. [1] tested the hypothesis that atherosclerosis detected at multiple sites provides important prognostic information in patients with and without cardiometabolic disorders followed for an average of 10.5 years from screening. In 1675 patients enrolled in the Multi Ethnic Study of Atherosclerosis (MESA), they performed computed tomography (CT) imaging of the coronary arteries and aorta and measured their respective calcium scores. They further measured the carotid intimal medial thickness (CIMT) and performed an ankle brachial index (ABI) on each one of the patients, of which 49% were affected by either the metabolic syndrome or diabetes mellitus. The results were remarkable and at once confirmatory and expanding on prior knowledge. The cardiovascular event rate was 10 folds higher in patients with all four abnormal atherosclerosis measurements compared to those without any abnormality. Although the 10-fold proportional risk was similar for all groups, the rate of events with 4 abnormal tests was lowest among patients without cardiometabolic disorders (35/1000 patients years), and highest among patients with diabetes mellitus (103/1000 patient years). The 10 fold increased risk was therefore similar to that of patients with a coronary artery calcium score (CAC) > 400 compared to patients with CAC = 0 [2]. The authors further showed that CAC was predictive of events even when the models were adjusted for all other measures of atherosclerosis, but the reverse did not hold true: once adjusted for CAC nothing else was predictive of events.

In C-statistic tests, the addition of measures of atherosclerosis provided incremental prognostic information over traditional risk factors and CIMT, aortic calcium and ABI, but not over CAC. Of interest, all measures of multisite atherosclerosis taken together provided the same incremental prognostic value as CAC alone. These observations showed that CAC is independent of and superior to all other measures of risk, be it traditional or imaging based.

CAC was absent in 723 of the 1675 patients; in 70% of the subjects without CAC there was no evidence of atherosclerosis at any site. Furthermore, in patients with no CAC, the presence of atherosclerosis at any other site was not predictive of cardiovascular events, highlighting the excellent negative predictive value of the absence of CAC.

What other lessons did we learn? There were more atherosclerotic sites in patients with cardiometabolic disorders than in subjects without. The risk of atherosclerosis in patients with diabetes mellitus was not associated with the level of hemoglobin A1c or metabolic syndrome, while it was associated with the duration of diabetes and the level of risk assessed via the pooled equations method. Patients with diabetes mellitus suffered higher event rates for any level of severity of atherosclerosis measure.

In summary, direct assessment of atherosclerosis is more predictive than traditional risk factors, and CAC appears to be superior to any other method or risk assessment tool, both to predict the occurrence of events and lack thereof.

Why then are we so resistant to implementing this simple imaging method that provides so much useful information? For years, the radiation exposure has been blamed as a limitation to its wide implementation. With today's technology, the exposure can be contained to below 1 milli-Sievert per scan. The chances of inducing a lethal cancer with such a low exposure, one third the amount of radiation we are exposed to from environmental sources in one year of life on earth, is infinitesimally small. Should this continue to be held as a reason to deny accurate risk assessment?

Professional organizations have not been forthcoming in supporting the use of CAC for risk assessment. However, very recently, the field received a significant boost from the publication of the new guidelines of the American College of Cardiology and American Heart Association on management of dyslipidemia [3]. The new guidelines embrace the use of CAC to both de-escalate risk in its absence, or increase the risk level in its presence. The recent guidelines further suggest that patients at intermediate or indeterminate risk might benefit most from CAC assessment. Interestingly, while the guidelines writers acknowledge the negative predictive value of CAC = 0, they state that this may not apply to individuals at particularly high risk, such as smokers and patients

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with diabetes mellitus. However, older data [4,5] as well as the present analyses [1] contradict this cautious approach. The “power of nothing” seems unbeatable by any other approach, and avoiding statins [6] or aspirin [7] may be appropriate in patients without CAC.

Cost of imaging is another frequent criticism leveled against the use of CAC for risk assessment. Recent data again appear to contradict this position. Hong et al. [8] modeled the cost of treating every patient with an indication for statin therapy, against the selective treatment of patients with CAC on a screening chest CT. The cost of long-term care was the same for the 2 methods, leaving room for patients and their physicians to discuss the preferred approach in a shared decision making fashion.

Next is the comment that: “I treat my patients in need of preventive efforts anyway, and there is nothing I can do for CAC, it does not go away”. There are several incorrect assumptions in these statements. Assuming that all physicians are excellent at implementing guidelines on risk reduction, almost half of the patients with an indication for statins have no CAC [9], hence they are at extremely low risk and do not need drugs [10]. At the same time, those with CAC, and especially patients with a CAC score > 100 [11], derive the greatest benefit from it. We need to treat 549 patients without CAC for 5 years to save one cardiovascular event [12],while we can save one event treating 12 patients with a CAC score > 100 [11]. Finally, CAC is a marker of risk and should not be seen as the target of therapy. A low creatinine clearance is a marker of renal impairment, but we are not correcting the clearance when we provide drugs to slow the progression of renal failure.

The most fatal flow of CAC detection for risk assessment, in the eye of physicians opposed to its use, is that there are no randomized clinical trials to demonstrate that by treating only patients with CAC, as opposed to those with an indication for treatment, the risk of events is reduced. However, the circumstantial evidence that this is true is overwhelming, and it is simply logical to predict that antibiotics will work best in patients with lobar pneumonia than in those at “risk of developing pneumonia”. Yet the dogma of randomized clinical trials, that reach a solid p-value nobody can dispute, may be too ingrained in the way we practice modern medicine to leave room for implementation of the obvious. Let's hope that the mounting evidence and the support of scientific associations may be sufficient for many more physicians to start implementing this simple algorithm: CAC present: higher risk; no CAC: minimal risk!

Conflict of interest

The author declared he does not have anything to disclose regarding conflict of interest with respect to this manuscript.

References

[1] Y. Zhao, M. Evans, M. Allison, et al., Multisite atherosclerosis in subjects with metabolic syndrome and diabetes and relation to cardiovascular events: the Multi-Ethnic Study of Atherosclerosis, Atherosclerosis (2019) 202–209.
[2] S. Malik, M.J. Budoff, R. Katz, et al., Impact of subclinical atherosclerosis on cardiovascular disease events in individuals with metabolic syndrome and diabetes: the multi-ethnic study of atherosclerosis, Diabetes Care 34 (2011) 2285–2290.
[3] S.M. Grundy, N.J. Stone, A.L. Bailey, et al., 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines, J. Am. Coll. Cardiol. (2018 Nov 8), https://doi.org/10.1016/j.jacc.2018.11.003 pii: S0735-1097(18)39034-X.
[4] P. Raggi, L.J. Shaw, D.S. Berman, et al., Prognostic value of coronary artery calcium screening in subjects with and without diabetes, J. Am. Coll. Cardiol. 43 (2004) 1663–1669.
[5] J.W. McEvoy, M.J. Blaha, J.J. Rivera, et al., Mortality rates in smokers and nonsmokers in the presence or absence of coronary artery calcification, JACC Cardiovasc Imaging 5 (10) (2012 Oct) 1037–1045 Erratum in: JACC Cardiovasc Imaging. 2013;6:747.
[6] K. Nasir, M.S. Bittencourt, M.J. Blaha, et al., Implications of coronary artery calcium testing among statin candidates according to American College of Cardiology/American Heart Association cholesterol management guidelines: MESA (Multi-Ethnic Study of Atherosclerosis), J. Am. Coll. Cardiol. 66 (2015) 1657–1668.
[7] M.G. Silverman, M.J. Blaha, M.J. Budoff, et al., Potential implications of coronary artery calcium testing for guiding aspirin use among asymptomatic individuals with diabetes, Diabetes Care 35 (2012) 624–626.
[8] J.C. Hong, R. Blankstein, L.J. Shaw, et al., Implications of coronary artery calcium testing for treatment decisions among statin candidates according to the ACC/AHA cholesterol management guidelines: a cost-effectiveness analysis, JACC Cardiovasc Imaging 10 (2017) 938–952.
[9] M.B. Mortensen, E. Falk, D. Li, et al., Statin trials, cardiovascular events, and coronary artery calcification: implications for a trial-based approach to statin therapy in MESA, JACC Cardiovasc Imaging 11 (2018) 221–230.
[10] V. Valenti, B. OH, R. Heo, I. Cho, et al., A 15-year warranty period for asymptomatic individuals without coronary artery calcium: a prospective follow-up of 9,715 individuals, JACC Cardiovasc Imaging 8 (2015) 900–909.
[11] J.D. Mitchell, N. Fergestrom, B.F. Gage, et al., Impact of statins on cardiovascular outcomes following coronary artery calcium scoring, J. Am. Coll. Cardiol. 72 (2018) 3233–3242.
[12] M.J. Blaha, M.J. Budoff, A.P. DeFilippis, et al., Associations between C-reactive protein, coronary artery calcium, and cardiovascular events: implications for the JUPITER population from MESA, a population-based cohort study, Lancet 378 (2011) 684–692.

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