Progression of Coronary Calcium Scores
Harder Gets the Evidence

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In this issue of *JACC*, Wong et al. (1) from the MESA (Multi-Ethnic Study of Atherosclerosis) report on accelerated progression of subclinical atherosclerosis as measured by coronary artery calcification (CAC) in apparently healthy individuals with the metabolic syndrome or diabetes. Limited evidence is available with regards to factors which accelerate progression of CAC and to that extent the current paper provides important guidance to clinicians who employ serial screening techniques to assess changes in risk or progressive disease states. The authors identified that diabetes was a major contributor to CAC progression; nearly one-quarter to one-third of patients with diabetes exhibited CAC progression, where in the coronary heart disease incidence rates were dramatically higher.

So, what is the take home message from this report? Certainly, the fact that diabetics are at high risk is not novel. Prior reports have noted that diabetics with CAC have a higher event rate than non-diabetics with CAC (2). Similarly, calcium score progression is already known to portend a worse prognosis (3). In a recent report by Min et al. (4) diabetes was associated with a 2.5-fold relative hazard for conversion of a 0 score to detectable CAC. Yet, as noted in the accompanying editorial by Kovacic and Fuster (5), the MESA cohort study continues to unravel important guidance as to defining risk in apparently healthy individuals. It should not go unnoticed that there remains a huge detection gap and that thousands of apparently healthy individuals die each year of cardiovascular disease without any prior warning or symptoms. Moreover, the epidemiological evidence continues to report that nearly one-half of sudden cardiac deaths occur in asymptomatic patients (6). However, many of our clinical databases often lack the depth of detail afforded to us in the MESA study (1).

Clinicians are frequently vexed with what to do with the CAC findings from a therapeutic intervention perspective. Moreover, there is a paucity of data on serial imaging and the paper by Wong et al. (1) is an effort to fill this niche. Following CAC progression is a logical and attractive strategy that is likely to affect clinical practice and improve stratification. Similar to previous findings in a mixed population, this paper shows that one can, using a relatively simple test like calcium score progression, further parse the risk in even high-risk groups. Not surprisingly, it is easy to get enthusiastic about such data. Despite accumulating data, however, clear limitations remain and calcium score progression has not yet reached prime time for routine clinical use. There is no consensus on the best way to reliably measure calcium score progression or how often it should be measured, and no agreement on how much change is significant (7). It also raises the question about what we do with the information in a high risk population—it probably does not change what we do for the subject at this time, and some successful therapies while reducing cardiac events, do not change or even worsen calcium scores, e.g. statins (8). Conceivably, therapy-induced alterations might limit our enthusiasm for the use of serial CAC testing for assessment of progression and given variable changes in plaque biology, it may make them even more difficult to interpret. Thus some have argued against an early adoption of this practice at this time (9). While it would

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be beneficial to iJACC readers to take the knowledge imparted by Wong et al. (1) and to integrate it into stratification, using it for targeted therapeutic intervention may be some distance away. There is currently an application before the NIH-NHLBI to randomize individuals to a CAC-guided intervention as compared to a Framingham risk score-guided intervention (principal investigator: Phil Greenland, MD). This should help facilitate wider application of CAC screening, if the role for guided preventive intervention was firmly established in a high quality randomized trial. It would be helpful if studies identified a patient subset(s) in whom targeted, intensive intervention was associated with a marked reduction in major adverse cardiovascular events. This would be similar to what was reported in the JUPITER (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin) trial, where, in a relatively healthy population statin therapy was associated with a 44% relative risk reduction in individuals with high hsCRP (10). We look forward to the next round of trials and cohort studies that are likely to provide harder evidence and further our understanding of atherosclerosis and cardiovascular risk.

REFERENCES