EDITORIAL

The Last Mile in Prevention—Can Coronary CT Angiography Help?

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We know how to prevent the majority of atherosclerotic cardiovascular disease (ASCVD), but this knowledge has not yet been translated into routine practice. Despite clear evidence that a healthy diet and physical activity improve cardiovascular outcomes, only a minority of adults adhere to these behaviors.[1] Similarly, inexpensive, effective therapies like statins prevent ASCVD in individuals at high risk of an event, and yet the vast majority of eligible individuals are not taking these therapies.[2] Without adoption of healthy lifestyle behaviors and/or proven preventive therapies, it is not surprising that cardiovascular mortality continues to rise.

Related article

There is no proven strategy to get prescribers to prescribe and patients to adhere to healthy behaviors and effective therapies. With the advent of imaging for subclinical atherosclerosis through coronary artery calcium (CAC) scoring or coronary computed tomography (CT) angiography (CCTA), a hypothesis has emerged that visual evidence of atherosclerosis will prompt both clinicians and patients to do what they are supposed to do, ie, prescribe and adhere to effective therapies and healthy behaviors. Several observational studies[3,4] have suggested that CAC scoring may help, and randomized clinical trials[5,6] have confirmed this effect. In the NOTIFY-1 (Incidental Coronary Calcification Quality Improvement Project) trial, informing individuals and their clinicians of incidental CAC on nongated chest CT scans led to a 7-fold increase in statin prescriptions.[5] In the recent CAUGHT-CAD (Coronary Artery Calcium Score: Use to Guide Management of Hereditary Coronary Artery Disease) trial, preventive care based on a CAC score in intermediate-risk individuals with a family history of coronary artery disease (CAD) led to a reduction in atherogenic lipids and coronary plaque progression compared with usual care.[6] However, it is unknown whether information from CCTA, which provides much more granular data on atherosclerosis phenotypes but requires contrast agent administration and has a higher radiation exposure, can improve risk factor modification.

In this issue of *JAMA Cardiology*, a nested substudy[7] of the Scottish Computed Tomography of the HEART (SCOT-HEART) 2 trial addresses this important point. The ongoing SCOT-HEART 2 trial (N = 6000) will evaluate whether screening for CAD with CCTA leads to reduction in coronary heart disease death or nonfatal myocardial infarction compared with standard screening using a CV risk score.[8] In this substudy,[7] the authors determined the association of CCTA with CV risk factors at 6 months compared with CV risk scoring. Asymptomatic individuals (N = 400) without known ASCVD but with at least 1 CV risk factor were randomized to the CCTA strategy vs the risk score–based strategy. Although all participants received lifestyle advice, those with any atherosclerosis on CCTA or a 10-year risk score of 10% or greater were recommended to initiate a moderate-intensity statin. Those in the CCTA arm with nonobstructive CAD were also recommended to initiate antiplatelet therapy (aspirin or clopidogrel, 75 mg, daily), and those with obstructive CAD were further recommended to initiate a high-intensity statin, consider initiation of renin-angiotensin-aldosterone system (RAAS)–inhibitor therapy, and consult with a cardiologist.

The substudy cohort was a relatively high-risk group: median 10-year risk was 15% in the risk score arm and 13% in the CCTA arm, of whom approximately half had atherosclerosis, with obstructive disease in 9%. With regard to the primary outcome, those in the CCTA arm were significantly more likely to meet the primary composite end point of achieving all National Institute for Health and Care Excellence (NICE) recommendations for diet, body mass index (BMI), smoking, and physical activity levels (17% vs 6%; odds ratio [OR], 3.42; 95% CI, 1.63-6.94; $P < .001$) over 6 months. The greatest differences were seen in diet compliance (47% vs 36%; $P = .03$) and BMI (31% vs 21%; $P = .04$, with BMI ranging from 18.5-25, calculated as weight in kilograms divided by height in meters squared); no differences were seen in smoking status or self-report of physical activity. Of note, the average daily step count was significantly higher in the CCTA group, even though self-reported achievement of physical activity targets did not differ between groups.

With respect to preventive therapies, fewer individuals were recommended to receive therapy in the CCTA arm compared with the risk score arm (51% vs 75%; OR, 0.34; 95% CI, 0.23-0.53; $P < .001$), but adherence was greater (77% vs 46%; OR, 3.86; 95% CI, 2.18-6.83; $P < .001$), resulting in similar proportions of participants using lipid-lowering therapy. Over 6 months, CCTA guidance led to greater improvements in weight, waist circumference, BMI, diastolic and mean blood pressure, low-density lipoprotein cholesterol level, and average daily step count but not in systolic blood pressure, high-density lipoprotein cholesterol level, triglycerides level, glycated hemoglobin concentration, or mental well-being. A nonrandomized comparison of higher-risk individuals (atherosclerosis on CCTA or risk score ≥10%) showed higher achievement of the primary end point (17% vs 4.5%; $P = .001$), along with greater improvements in weight, waist circumference, BMI, use of lipid-lowering, antiplatelet, and RAAS inhibitor therapies, blood pressure and lipid parameters, and average daily step count. Interestingly, outcomes were similar in those randomized to receive a verbal CCTA report vs a visual report with CCTA images.

Some caveats should be noted. Despite the significant increase in achievement of NICE lifestyle recommendations,

83% of participants in the CCTA arm still did not achieve this goal. Further, the improvements in blood pressure and lipids were statistically significant but modest. The most clinically relevant improvements appeared to be in dietary compliance, BMI changes, step count, and use of preventive therapies. Outcomes were assessed at the relatively short time point of 6 months, and it is unclear if these benefits would be sustained longer term or if there are downstream unintended consequences. More importantly, the impact on clinical events is unknown but will be assessed by the larger, ongoing trial. The study population was a relatively homogenous group from Scotland, and several points indicate that this was likely a privileged and/or motivated group of individuals, beyond the fact that they agreed to participate in a clinical trial. Most were university educated, nonsmokers, and with an average pretrial step count of more than 7000 steps per day, far greater than the average step count of 5000 for individuals globally.[9] Whether CCTA would influence behavior in a more diverse and/or less motivated group of individuals remains to be seen.

These limitations notwithstanding, the results of this nested randomized clinical trial within the SCOT-HEART 2 study are striking. A preventive strategy incorporating CCTA appeared to be not only more precise but also more motivating to participants and clinicians. CCTA reclassified 1 in 3 individuals based on 10-year risk score, targeting therapy to those who were assumed to derive greatest benefit (although this has yet to be proven and will be evaluated in the ongoing trial). Increased precision of risk prediction with subclinical atherosclerosis compared with risk scores has been shown in prior observational studies[10,11] and is logically intuitive: an assessment of subclinical atherosclerosis incorporates all risk factors, both known and unknown, innate and acquired, traditional and nontraditional, measurable and unmeasurable. It also visualizes the actual presence of disease at the time of the scan, rather than postulating the population-based probability of a future event. Indeed, the recent "The Lancet Commission on Rethinking Coronary Artery Disease: Moving From Ischemia to Atheroma" advocates for a paradigm shift away from risk-based scoring toward active screening for asymptomatic atherosclerosis.[12]

Why does detection of atherosclerosis with CCTA better motivate individuals to make lifestyle changes and take preventive therapies than risk prediction scores? As the authors note, this may be related to the Health Efficacy Belief model, in which awareness of atherosclerosis increases an individual's perceived susceptibility to the disease, self-efficacy, and intentions for behavior change.[13] Interestingly, knowledge of the presence of atherosclerosis appeared to be the critical factor; visualization of the atherosclerosis did not lead to further benefit. Whether this is true in populations with different levels of education, health literacy, and trust in the medical system is unknown. Another contributing factor could be a general misperception of personal CV risk. In the Patient and Provider Assessment of Lipid Management (PALM) Registry, there was no correlation between patients' estimates of their 10-year CV risk and their calculated CV risk.[14] Understanding estimated risk is abstract and hard; understanding the presence of atherosclerosis is not.

This study adds to the growing literature that supports screening for subclinical atherosclerosis to guide risk factor management. What remains unknown is (1) the optimal method to implement such screening and (2) whether such screening will improve clinical outcomes. Both these questions are the subject of a recent Notice of Funding Opportunity from the National Heart, Lung, and Blood Institute to test screening and management strategies to reduce progression of atherosclerotic plaque in younger individuals with low calculated 10-year risk. One critical question is whether the optimal screening strategy should include CCTA or whether CAC scoring is sufficient. This has significant public health implications, as CAC scores are cheaper, require less radiation, and do not use contrast. On the other hand, CCTA provides more detailed information about plaque morphology and subsequent risk and captures those individuals with only noncalcified plaque who tend to be younger.[15]

In the end, we can continue to do what we have always done: provide preventive recommendations based on calculated risk scores. But if most patients and their clinicians are not sufficiently motivated by these scores to make lifestyle changes or prescribe preventive therapies, what is the point? The authors of this SCOT-HEART 2 substudy should be congratulated for providing compelling data that CCTA, and screening for subclinical atherosclerosis in general, may help us cross the last mile to effectively prevent ASCVD.

ARTICLE INFORMATION

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