Editorial

Coronary Artery Calcium Scores Using Nongated Computed Tomography
What to Do With Incidental Results?

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The coronary artery calcium (CAC) score is well established as a potent marker of increased cardiovascular risk that significantly improves risk prediction beyond traditional risk factors. A CAC score \( >300 \) has been shown to confer a 10-fold increase in the risk for a cardiovascular event compared with adults with a CAC of 0.\(^1,2\) The improvement in risk prediction is substantially greater with CAC than other imaging and serum markers of subclinical cardiovascular disease.\(^3,4\)

The cohort studies that have most informed our understanding of coronary calcium measured CAC scores with dedicated cardiac computed tomography (CT). Image acquisition was gated to diastole to minimize motion artifact and to decrease the likelihood that regions of CAC were missed. However, most chest CTS done for clinical purposes are ordered primarily to assess the lungs and other structures in the chest and thus are not gated. Without gating, there is a concern that assessment of CAC is not accurate.

Rather than disregard readily available data, several investigators have sought to determine whether information about CAC burden from nongated CTS can be used effectively to predict cardiovascular risk. In this issue of *Circulation: Cardiovascular Imaging*, Xie et al\(^5\) compiled data from several studies to determine the validity and prognostic value of CAC scoring obtained on nongated thoracic CT scans. To assess the diagnostic performance, the authors performed a meta-analysis of 5 studies that directly compared CAC scores obtained using gated versus nongated CTS. The patient populations in the studies varied, with some representing adults consecutively referred for a chest CT, positron emission tomography, or single-photon emission CT; others were specifically referred for lung cancer screening because of their smoking history. Whereas the CAC score on a gated CT is typically calculated using the Agatston method (which incorporates the Hounsfield units and area of each calcified plaque), most of the studies in the analysis by Xie et al\(^5\) used various semiquantitative techniques and grouped the scores into categories.

Overall, there was excellent agreement between the gated and nongated CAC scores, with a pooled correlation coefficient of 0.94 (95% confidence interval, 0.89–0.97). However, the episodes of discordance between the gated and nongated results are important to note. Fifty-five adults (8.8%) were found to have a CAC \( >0 \) on the gated images but showed no calcification on the nongated images. Most with a false negative (52 of 55) had CAC scores on the lower end, ranging from 1 to 100. The most common misclassification was among adults with an Agatston score \( >400 \). A nongated CT underestimated the CAC score for \( \leq 20\% \) of those participants, although most had scores of 100 to 400. Overestimation of the CAC score using nongated CT was rare. Only 2.6\% of those with a CAC score \( >400 \) on nongated CT were found to have a lower score on gated CT. In total, the results suggest that a positive CAC score from a nongated CT can usually be trusted and that a CAC score of 0 is not definitive from a nongated CT.

Xie et al\(^5\) then performed a systematic analysis of 5 studies (including 34,028 adults) that examined whether CAC quantification using nongated CT scans was associated with future cardiovascular events. The authors did not conduct a meta-analysis because of the heterogeneity in CAC scoring methods and outcomes. About 70% of the patients were referred for CT for lung cancer screening. The adjusted hazard ratios for an event among adults with the highest category of CAC (corresponding to a CAC of \( >400 \) or \( >1000 \), depending on the study) ranged from 2.1 to 5.3. Although statistically significant, the hazard ratios are smaller than those seen in cohort studies that used gated CT.\(^1,2\) Xie et al\(^5\) proposed potential explanations, including that many adults in the reference category (CAC=0) likely had some CAC that was missed because the image acquisition was performed without gating. Other issues to consider are that follow-up for many of the participants was \(<2\) years and 2 of the studies had \(<50\) events.

To us, the most important question is whether the findings of Xie et al\(^5\) are compelling enough to change clinical practice. We feel that they are. To be sure, reporting of CAC burden on nongated chest CTS has likely become standard in many places, but it is far from universal. Even with the limitations of the studies above, assessment of CAC burden identified adults at a substantially elevated risk of a cardiovascular event. Detection of CAC should therefore be treated as any other incidental finding with important prognostic information. However, if the clinical suspicion of coronary artery disease is high, the absence of CAC on a nongated CT should not be used as reassurance. The techniques used to quantify CAC in the present review did not require additional imaging, were
not time-consuming, and could be reasonably integrated into clinical practice. Furthermore, 1 study compared CAC scoring between radiologists with and without training in cardiac imaging and found excellent agreement, with an interobserver correlation coefficient of 0.93.3

Routine reporting of the CAC score seen on nongated chest CTs could affect millions of people. From the results of recent studies such as the National Lung Screening Trial (NLST),7 the American College of Chest Physicians, the American Society of Clinical Oncology, and the American Thoracic Society endorse annual screening for lung cancer with low-dose chest CT among adults who would have qualified for the NLST: men and women 55 to 74 years of age who are currently smoking or who had quit smoking within the past 15 years with a ≥30-pack-year history.8 It is estimated that 7 million Americans would be eligible for such screening,7 a number that of course does not include the millions of additional adults who undergo a chest CT for other reasons. Given the strong association between smoking and cardiovascular risk, it is not surprising that the prevalence of CAC >0 was well over 50% in many of the studies included in the present analysis, and the proportion of people with extensive CAC (similar to an Agatston score ≥400) was ≈20%.

Despite temporal trends showing improvement in the control of cardiovascular risk factors, it is estimated that more than half of US adults still do not have optimal levels.9,10 In a study of adults referred for lung cancer screening, Jacobs et al11 found that >40% of those with a CAC score >1000 were not taking antihypertensive or statin therapy, despite many having elevated blood pressure or cholesterol levels. Knowledge of CAC scores in patients referred for CAC testing has been shown to be associated with an increase in physician prescription and patient adherence to aspirin and blood pressure– and cholesterol-lowering medications and the adoption of therapeutic lifestyle changes.12–14 Showing patients sample images from their scans is thought to serve as a powerful visual tool to help motivate behavior change. However, it is not yet known whether diagnosing coronary atherosclerosis as an incidental finding on a chest CT will also result in improved attention to coronary heart disease risk factors or better patient outcomes, so some concern about this approach is in order.

Many other questions remain regarding how CAC should be used in the clinical setting, particularly as it relates to pharmacological therapy. Does treatment of risk factors based on CAC testing reduce cardiovascular events? Should all such patients with incidentally diagnosed CAC be treated with preventive medications such as aspirin or statins, or only those with the highest scores? Should CAC be used to initiate pharmacological therapy for adults who would not otherwise qualify on the basis of current guidelines? What is the most effective way to communicate unexpected CAC results? These questions warrant further study. However, the findings of Xie et al provide an important opportunity that should not be ignored.

References

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