Atherosclerotic cardiovascular diseases remain the number one killer in the world, accounting for nearly one-third of all deaths worldwide. There is a clinical dilemma, in that almost half of acute coronary events occur in previously asymptomatic patients, and nearly 70% of acute coronary events result from coronary lesions that are not hemodynamically significant or flow-limiting before the event. Thus, it is important to identify patients at risk for future cardiovascular events. Multiple scoring systems have been developed to predict the risk of coronary events in patients who do not have a history of cardiovascular diseases, but are at risk for future events. The Framingham risk score (FRS) is probably the most extensively adopted one. The main problem for FRS, is that it does not incorporate family history and many components of metabolic syndrome. Furthermore, it has been reported that more than 60% of coronary atherosclerotic events occurred in patients who were in low- or intermediate-risk categories. It would be important to look for other imaging modalities, to identify patients in the intermediate FRS group, who may have increased risks of coronary events.

The coronary artery calcium (CAC) score, obtained by CT scan, has become useful in providing additional prognostic information independent of FRS. In a study involving 3529 asymptomatic patients from the Framingham Offspring Cohort, applying CAC scoring, re-classified the low and intermediate FRS risk patients into lower- and higher-risk strata. What is more interesting is the prognostic value of the CAC score of zero. The issue has been intensively debated in recent years. The negative predictive value of zero CAC score critically depends on the presence of symptoms. In a cohort of 25,253 consecutive asymptomatic individuals for CAC, scanning, the 10-year survival was 99.4% for patients with zero CAC score. In a recent meta-analysis involving more than 29,000 asymptomatic patients with a zero CAC score, with a mean follow-up period of 50 months, the annual event rate was only 0.12%. A zero CAC score was more reassuring than a negative intima-media thickness test or negative stress test to be protective from cardiovascular events. Furthermore, diabetic patients who had a zero CAC score had a similar cardiovascular risk to those without diabetes.

For symptomatic patients, the absence of CAC is unable to exclude obstructive coronary artery disease. This has been demonstrated in a sub-study of 291 patients from the CORE64 multicenter trial, comparing the diagnostic performance of 64-detector computed tomography to conventional angiography. From a total of 383 vessels without any CAC, 47 (12%) presented with ≥50% stenosis; from a total of 64 totally occluded vessels, 13 (20%) had a zero CAC score. It is widely accepted that in a symptomatic population with clinical evidence of myocardial ischemia, a CAC score of zero is not totally reassuring, because both obstructive and non-obstructive coronary artery disease can occur in the absence of calcification. CAC predicts events based on the overall atherosclerosis burden rather than the detection of vulnerable or obstructive plaques.

In the current issue of the *Journal of the Chinese Medical Association*, Chun-Ku Chen et al report the frequency of atherosclerotic plaques in patients with a zero CAC score; they also report their investigation of associated risk factors. The demographic data, cardiovascular risk factors and imaging features in 519 consecutive patients were retrospectively analyzed. Coronary plaques were found in 66 (12.7%) of patients, and significant coronary artery stenosis, defined by >50% luminal narrowing, was found in 6 patients (1.2%). By multivariate logistic regression analysis, age >55 years and body mass index >27 were found to be independent predictors for the presence of plaques. Chen et al found coronary plaques in a significant proportion of individuals with a zero CAC score. In this study, chest pain was complained by only 12.7% of patients, and only 3% of patients belonged to the high-risk group by FRS. Unfortunately, there were no follow-up data regarding cardiovascular events in these patients. It would be difficult to conclude that they would have a high cardiovascular risk. In fact, these patients might have a very low cardiovascular risk, despite the presence of coronary plaques. It should be re-iterated that CAC predicts cardiovascular events based on the overall risk, instead of the detection of vulnerable plaques. Since the significance of zero CAC score in Taiwanese patients is unknown, it would be interesting to perform a large-scale prospective study in both symptomatic and asymptomatic patients to determine the prognostic value of a zero CAC score in Taiwanese patients. The information about independent predictors would then become valid.
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