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REVIEW

STATE-OF-THE-ART PAPER

The Case For and Against a Coronary Artery Calcium Trial

Means, Motive, and Opportunity

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CME Objective for This Article: After reading this article the reader should be able to: 1) review the evidence in support of coronary artery calcium imaging to reclassify personalized estimates of future atherosclerotic cardiovascular disease risk in primary prevention adults; 2) understand how accurate prediction of personalized atherosclerotic cardiovascular disease risk is important in the treatment of hypercholesterolemia for the prevention of atherosclerotic cardiovascular disease; and 3) discuss the desired level of evidence needed to justify more widespread use of CAC imaging as a screening tool for atherosclerotic cardiovascular disease.

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ABSTRACT

Numerous observational studies have shown that coronary artery calcium (CAC) imaging can improve cardiovascular risk assessment in asymptomatic adults. Whether CAC imaging can improve cardiovascular outcomes as part of an overall risk reduction strategy compared to alternative care approaches has not been demonstrated in clinical trials. Therefore, the role of CAC imaging in primary prevention of cardiovascular disease is somewhat contentious. Advocates for expanded CAC testing offer the large amount of observational data as support for their position, while opponents to wider CAC testing propose that only a clinical trial can resolve the matter. This paper reviews the arguments for and against such a trial based on clinical, safety and economic considerations. We also propose potential trial approaches based on recent changes in clinical practice that could make a new CAC trial design feasible. (J Am Coll Cardiol Img 2016;9:994–1002)

Coronary artery calcium (CAC) imaging with noncontrast cardiac computed tomography (CT) is endorsed in the 2013 risk assessment guideline from the American College of Cardiology (ACC) and the American Heart Association (AHA) to enhance atherosclerotic cardiovascular disease (ASCVD) risk estimation and facilitate statin allocation decisions when the need for statin therapy remains uncertain after a clinician-patient risk discussion (1,2). This endorsement is tepid, with a IIb recommendation ("may be considered"), mostly due to the absence of any adequately powered, prospective, randomized trials of CAC-guided ASCVD prevention strategies or protocols (inclusive, for example, of lifestyle changes, statins, or aspirin). Indeed, despite the fact that CAC imaging has an abundance of supportive observational data, no definitive outcomes trials have been reported to date (hereafter termed "CAC trial") (3). In this review, we discuss the pros and cons of a CAC trial; with each position framed in the context of clinical, safety, and economic considerations of CAC testing. We also suggest potential solutions to a number of challenges that have hampered prior efforts to perform a CAC trial.

CLINICAL CASE FOR A CAC TRIAL

Why perform a CAC trial? In the current era of personalized medicine, there is an increasingly recognized need to improve upon the traditional cardiac risk-factor based paradigm of estimating ASCVD risk (4). Current 2013 ACC/AHA cholesterol treatment guidelines recommend a 10-year estimated ASCVD risk score as an important metric to assess eligibility for statin therapy in primary prevention (1,5). ASCVD risk estimation is heavily influenced by age, and approximately one-half of the U.S. primary prevention adult population is now eligible for statin therapy (58 million adults, an increase of 13 million from prior guidelines) (6). In addition, a number of reports have suggested that the new ASCVD risk calculator may overestimate risk for the individual (7,8). This has led to concerns for statin overuse (9). Methods to improve the individual accuracy of ASCVD risk estimates, thereby personalizing statin allocation, would be highly desirable.

In this context, CAC, which is a highly specific marker of atherosclerosis, has emerged as the most robust and reliable method with which to reclassify ASCVD risk (10,11). Population-based observational cohort studies have demonstrated higher absolute and relative ASCVD event rates among persons with elevated CAC (12–14). CAC is a direct measure of the cumulative effect of known and unknown risk factors on the vasculature with respect to atherosclerosis and is fundamentally different from risk factor-based assessment (4). Furthermore, the absence of CAC on imaging is common (with a 50% prevalence in asymptomatic, general population, U.S. adults, for example) (12) and can even be found among