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# Calculating Risk vs Detecting Disease:

## Changing the Cardiovascular Prevention Paradigm Using Cardiac CT*

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### Keywords

cardiovascular risk; coronary artery calcium score; coronary artery disease; coronary atherosclerosis; coronary computed tomography angiography (CTA); plaque; prevention

Disease prevention is founded on the principle that early and accurate detection coupled with risk-appropriate, effective interventions reduce morbidity and mortality in individuals and populations. In cardiovascular medicine, detection of subclinical coronary artery disease (CAD) using low-radiation, noncontrast, coronary artery calcium (CAC) scans has been consistently shown to be more accurate than probabilistic risk scores for assessing atherosclerotic cardiovascular disease (ASCVD) risk.[1] CAC scans identify patients who are likely to derive the most benefit from statins and aspirin, and they better motivate patients to make therapeutic lifestyle changes compared with usual care.[2-4] The U.S. Preventive Services Task Force, however, recommends against CAC testing, and current cardiovascular prevention guidelines consider CAC scans useful in select patients at intermediate 10-year ASCVD risk.[5,6] Critics of CAC testing and the United States Preventive Services Task Force point to an absence of large-scale, randomized clinical trials that show reduction in hard clinical events using CAC-guided prevention vs usual care while embracing less accurate risk scores that have also not been shown to improve outcomes in prospective comparative effectiveness trials.

Coronary computed tomography angiography (CTA) offers a potential advantage over CAC scans by depicting the burden of both calcified and noncalcified atherosclerosis, including “high-risk” plaque features, as well as stenosis. In studies involving symptomatic patients, coronary CTA has been shown to be more accurate than CAC for coronary plaque detection and event prediction.[7,8] Recent advances in CT technology allow its performance at radiation doses equivalent to CAC testing in many patients while using low iodinated

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contrast volumes.[9] Given these advances and emerging software tools for whole-heart plaque quantification, the utilization of coronary CTA in asymptomatic patients as a more informative decision tool than CAC or risk factors, and to potentially identify high-risk stenosis, is an active area of investigation. However, population-based studies assessing CAD burden in asymptomatic patients using coronary CTA are limited, and significant concern exists regarding the risk of increased resource utilization (eg, catheterizations, revascularizations), and possible harm, in patients with incidentally discovered stenosis.

In this issue of *JACC: Cardiovascular Imaging*, Nasir et al[10] performed a cross-sectional study to assess the subclinical burden of CAD using CAC and coronary CTA in 2,359 asymptomatic subjects between 40 and 65 years of age (mean age: 53 years) living in the greater Miami, Florida, area. In addition to its geographic clustering, the study cohort was not representative of the general U.S. population in many other ways: 79% had a college degree, most were at high socioeconomic status, nearly one-half were of Hispanic/Latino ethnicity (47%), and almost all were remarkably healthy. Specifically, 73.9% of subjects were at <5% 10-year ASCVD risk according to the pooled cohort equation, only 3% were active smokers, and none had a serum creatinine level >1.5 mmol/L.

Despite the very-low-risk cohort, roughly one-half of the subjects had subclinical CAD on coronary CTA.[10] Specifically, coronary atherosclerosis was present in 42% measured by using CAC testing (>0) and 49% had evidence of CAD on coronary CTA, with 25% of subjects having plaque involving at least 3 coronary segments (segment involvement score ≥3); high-risk plaque features were uncommon (7% of subjects). Among those at <5% and 5% to <7.5% 10-year risk (groups not typically recommended for statin therapy), 31.5% and 74.7% had evidence of subclinical CAD, respectively. In those with CAC = 0, coronary CTA identified 16% with evidence of subclinical CAD, a greater prevalence of which was noted among subjects at higher ASCVD risk (Table 1). Of note, ~40% with CAC = 0 and coronary CTA–defined plaque had multiple segment involvement (segment involvement score ≥2). Not surprisingly, significant stenosis was uncommon in the overall cohort, with 4.1% and 1.8% with maximum stenosis 50% to 69% and >70%, respectively, and it was particularly rare in those at low ASCVD risk or CAC = 0. Finally, radiation doses were low, with a mean radiation dose from CAC and coronary CTA of ~1.0 mSv and 1.87 mSv.

The results of this important study,[10] documenting the high burden of subclinical ASCVD in a very-low-risk U.S. population, serve to challenge prevention strategies primarily guided by population-derived probabilistic risk scores. These results are similar to the recently published SCAPIS (Swedish Cardiopulmonary Bioimage Study) trial in which coronary CTA was performed in >25,000 low-risk, asymptomatic adults without known ASCVD in Sweden (mean age: 57 years).[11] In SCAPIS, 42% of adults had coronary CTA-detected atherosclerosis, whereas stenosis ≥50% was rare (5.2%). In this population, among those with CAC = 0, evidence of plaque on coronary CTA was noted in 5.5%, a finding rising to 9.2% among those at intermediate 10-year ASCVD risk (Table 1). The SCAPIS authors[11] concluded that subclinical CAD is highly prevalent and that CAC = 0 does not exclude atherosclerosis, particularly in those with higher baseline risk.

## IS THERE A ROLE FOR CORONARY CTA IN ASYMPTOMATIC PATIENTS?

It is clear that coronary CTA will detect more disease than CAC. In the current study by Nasir et al,[10] roughly 1 in 6 patients with CAC = 0 had evidence of CAD on coronary CTA, frequently involving >1 coronary segment. These findings align with data from symptomatic studies, such as PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) and SCOT-HEART (Scottish Computed Tomography of the HEART), where ~16% of individuals with CAC = 0 had plaque.[8,12] In a symptomatic population from Western Denmark, coronary CTA-identified plaque and stenosis (≥50%) despite CAC = 0 was associated with increased risk (HR: 1.80; 95% CI: 1.02-3.19) of myocardial infarction or death over 4.3 years in patients aged <60 years.[13] In the Miami Heart Study, while the overall disease burden in those with CAC = 0 was low (most with a segment involvement score = 1), coronary CTA-identified plaque paired with early changes in preventive therapies and lifestyle may translate to lower long-term events. However, studies assessing changes in hard outcomes after CT-guided prevention vs usual care are currently lacking.[10]

There is, of course, significant concern about coronary CTA-identified stenosis leading to more testing and unnecessary revascularization. We eagerly await data on how coronary CTA influences rates of downstream testing, changes in medications, and lifestyle, and the impact of incidental findings on care and costs in the Miami Heart Study. Although stenosis ≥50% is a marker of increased risk, it is unlikely that this risk is reduced by coronary revascularizations in an asymptomatic, low-risk population. If coronary CTA is used in asymptomatic patients, it should be stressed that stenosis be decoupled from tests for ischemia or evaluations for revascularization except in examples of clearly high-risk CAD (eg, left main ≥50%). Hence, for coronary CTA to function as an effective test in asymptomatic adults, significant education would be required to ensure that patients and providers do not invoke the “oculostenotic reflex” but rather understand that its goal is plaque detection and quantification. We look forward to future work from the Miami Heart group that explores the potential prognostic value of plaque quantification, as well as ongoing randomized clinical trials in this area, such as the SCOT-HEART 2. In the meantime, we are confident that CT-guided prevention, using CAC (and potentially coronary CTA), provides the optimal approach to personalized cardiovascular preventive care.

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## TABLE 1

Comparison of Select Demographic Characteristics, CAC Scores, and Coronary CTA Results in the Miami Heart and SCAPIS Studies

| | Miami Heart Study (n = 2,359) | SCAPIS (n = 25,014) |
|---|---|---|
| Demographic characteristics | | |
| Female | 1,170 (49.6) | 12,666 (50.6) |
| Age, y | 53.4 ± 6.8 | 57.4 ± 4.3 |
| Education, university degree | 1,871 (79.3) | 11,263 (45.8) |
| Employed | 2,359 (100) | 20,952 (83.2) |
| CAC scores[a] | | |
| 0 | 1,375 (58) | 14,957 (59.8) |
| Mild | 669 (28) | 17,211 (69.4) |
| Moderate | 315 (13) | 2022 (8.1) |
| Severe | 141 (6) | 881 (3.5) |
| Coronary CTA-based plaque features | | |
| Any plaque | | |
| Overall | 1,155 (49) | 10,508 (42) |
| CAC = 0 | 223 (16.2) | 818 (5.5) |
| Any stenosis ≥50% | | |
| Overall | 1,317 (5.2) | 120 (5.9) |
| CAC = 0 | 11 (0.8) | 63 (0.4) |
| % of subjects with CAC = 0 and any plaque by coronary CTA, stratified by 10-year ASCVD risk score | | |
| <5% | 13.5 | 4.4 |
| ≥5 to <7.5% | 26.8 | 5.3 |
| ≥7.5 to 20% | 30.1 | 9.2 |
| ≥20% | 50 | 15 |

Values are n (%) or mean ± SD, unless otherwise indicated.

[a]Mild = >0 to <100; Moderate = ≥100 to 300 in the Miami Heart Study cohort and ≥100 to 400 in the SCAPIS (Swedish Cardiopulmonary Bioimage Study) cohort; and Severe = ≥300 in the Miami Heart Study cohort and ≥400 in the SCAPIS cohort.

ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium; CTA = computed tomography angiography.