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Selective Use of Coronary Artery Calcium Testing for Shared Decision Making: Guideline Endorsed and Ready for Prime Time

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The use of traditional risk factors and laboratory markers to estimate 10-year risk for atherosclerotic cardiovascular disease (ASCVD) remains the cornerstone of clinical decision making for primary prevention of ASCVD in asymptomatic persons. In the United States, risk estimation begins with the pooled cohort equations, which were first introduced in the 2013 American Heart Association and American College of Cardiology (AHA/ACC) prevention guideline. The new 2018 AHA/ACC guideline still recommends use of these equations as a prudent first step in clinical decision making, despite acknowledging that they provide only moderate risk discrimination and may overestimate risk (1, 2).

Since publication of the paradigm-shifting 2013 guideline, concern has been raised that risk overestimation could lead to statins being recommended to many patients who are less likely to receive net benefit from therapy. For patients at either high or very low risk for ASCVD, imprecise risk estimation may not be clinically relevant. However, for all other patients, using the pooled cohort equations as a standalone risk assessment tool may be insufficient for definitive decision making.

The 2018 AHA/ACC risk assessment and cholesterol management guideline acknowledges the limitations of traditional risk prediction. It recommends considering additional clinical factors and other tests to more accurately assess cardiovascular risk for many adults with 10-year risk for ASCVD between 5% and 20% (3, 4). The presence of these "risk enhancers," such as a family history of premature ASCVD, South Asian ancestry, inflammatory biomarkers, HIV infection, and rheumatologic disease, can increase risk (3, 4). However, as their name indicates, risk enhancers are only valuable for identifying persons who may be at higher risk than otherwise expected. Their absence does not reclassify risk downward, and borderline- to intermediate-risk patients—especially those with no traditional risk factors—may still face risk overestimation and potential overtreatment.

The 2018 AHA/ACC prevention guideline offers something fundamentally new for these patients. For more definitive risk stratification (that is, to move patients both up and down the risk spectrum), the guideline explicitly states, "identification of subclinical atherosclerosis rather than use of serum biomarkers is preferred, because of the extensive body of evidence demonstrating the superior utility of atherosclerosis disease assessment" (3, 4).

When evaluating subclinical atherosclerosis, coronary artery calcium (CAC) testing is preferred over other imaging methods. Measuring CAC has proved consistently better at prognosticating, discriminating, calibrating, and reclassifying ASCVD than using traditional risk scores. The most notable studies, such as MESA (Multi-Ethnic Study of Atherosclerosis) and the Heinz Nixdorf Recall Study, showed that persons with severe CAC had 9- to 16-fold higher hazard ratios than those with a CAC score of 0 (5).

Imaging studies are unique in their superior sensitivity for clinically important atherosclerosis. Tests with high sensitivity are ideally suited for downwardly modifying posttest risk estimates; imaging tests for subclinical atherosclerosis are thus ideal for identifying persons at very low risk for ASCVD (a concept known as the *imaging hypothesis* of risk prediction) (6). Thus, apart from the ability of CAC testing to identify those truly high-risk persons in whom most ASCVD events occur, an absence of CAC confers a very low risk for future events. A CAC score of 0 has been established to reclassify borderline- to intermediate-risk patients into a category in which lipid-lowering therapy is no longer recommended (7). Furthermore, among the wide range of negative risk markers—including low high-sensitivity C-reactive protein levels, a normal ankle–brachial index, and a lack of carotid plaque—the absence of CAC results in the greatest risk reduction and downward reclassification of risk (8), a concept termed *the power of zero CAC* (9).

The new 2018 AHA/ACC prevention guideline has thus assigned a class IIA recommendation for CAC testing to aid uncertainty around risk estimates in selected borderline- and intermediate-risk patients (that is, those with a 10-year risk for ASCVD between 5% and 20%) aged 40 to 75 years in order to guide individualized management decisions (3, 4). For the first time, the guidelines have acknowledged the power of a CAC score of 0 among patients in whom intensive statin therapy is of limited value and may be avoided.

Of note, up to 50% of patients with a 10-year risk for ASCVD between 5% and 20% have a CAC score of 0 and may have flexible treatment goals (7). Approximately 25% of these patients have extensive CAC (score ≥100), and their 10-year risk for ASCVD is in a range where the "benefit of statin therapy clearly exceeds potential for harms." Statin therapy should also be strongly considered in those with a CAC score between 1 and 99. In all patients, "clinical judgment and patient preferences should guide decision-making" (3).

It is critical that the main stakeholders, especially primary care physicians, understand the newly proposed role for CAC testing and do not equate it with screening. Rather than bringing in many additional statin candidates, this testing should serve as a decision aid to "de-risk" certain patients and distinguish those who may benefit from preventive pharmacologic therapies (6–9).

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Table. CAC Testing

Indication
- Primary prevention (no previous clinical ASCVD) in asymptomatic patients
- Borderline- and intermediate-risk patients (predicted 10-y ASCVD risk, 5%–20%)
- After clinician–patient discussion if further risk stratification is desired

Results
- CAC score of 0: May withhold or delay statin therapy
- CAC score between 1 and 99: Favors statin therapy
- CAC score ≥100 or in the ≥75th percentile: Statin therapy indicated
- Heart-healthy lifestyle interventions are indicated for all
- Avoid downstream testing, including coronary angiography, for asymptomatic patients

Repeated testing
- Can be considered in 5 y if the CAC score is 0 or 1–99

Radiation exposure
- Approximately 1 mSv (similar to bilateral mammography)

Costs
- $50–$350 out of pocket; not currently reimbursed by most insurance payers
- Cost-effective and potentially cost-saving if applied to intermediate-risk patients and considering pill disutility

ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium.

The updated 2018 AHA/ACC risk assessment and cholesterol management guideline strongly endorses selective CAC testing, but the decision to use this testing is not always straightforward. The approximate average national cost of CAC testing is between $50 and $350, and additional downstream testing for noncardiac incidental findings (such as lung nodules) can generate recommendations for follow-up imaging in approximately 5% of adults without a history of smoking. However, recent analyses have been reassuring in that selective use of statin therapy in those with CAC–instead of recommending it as a "treat-all" approach in intermediate-risk patients–is cost-effective, even when these additional upfront costs are accounted for (10). Moreover, the modest radiation exposure (0.9 mSv compared with yearly average background radiation exposure of 3 mSv) must be discussed with patients to allow for informed decision making.

The next step for CAC testing in primary prevention is clearly universal coverage for appropriate candidates to ensure equal access. We must advocate for reasonable pricing (<$150). We also must reinforce that CAC testing is a decision aid and should almost never be followed by downstream cardiovascular testing, such as stress testing or cardiac catheterization.

In summary, CAC testing is now a guideline-endorsed decision aid for borderline- to intermediate-risk patients who seek more definitive risk assessment as part of a clinician–patient discussion (Table). This testing can reduce low-value treatment and focus primary prevention therapy on those most likely to benefit.

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References

1. **DeFilippis AP, Young R, Carrubba CJ, McEvoy JW, Budoff MJ, Blumenthal RS, et al.** An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. Ann Intern Med. 2015;162:266-75. [PMID: 25686167] doi:10.7326/M14-1281
2. **Cook NR, Ridker PM.** Calibration of the pooled cohort equations for atherosclerotic cardiovascular disease: an update. Ann Intern Med. 2016;165:786-94. [PMID: 27723890] doi:10.7326/M16-1739
3. **Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al.** 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018. [PMID: 30423393] doi:10.1016/j.jacc.2018.11.003
4. **Lloyd-Jones DM, Braun LT, Ndumele CE, Smith SC Jr, Sperling LS, Virani SS, et al.** Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease: a special report from the American Heart Association and American College of Cardiology. J Am Coll Cardiol. 2018. [PMID: 30423392] doi:10.1016/j.jacc.2018.11.005
5. **Greenland P, Blaha MJ, Budoff MJ, Erbel R, Watson KE.** Coronary calcium score and cardiovascular risk. J Am Coll Cardiol. 2018;72:434-47. [PMID: 30025580] doi:10.1016/j.jacc.2018.05.027
6. **Blaha MJ, Blumenthal RS, Budoff MJ, Nasir K.** Understanding the utility of zero coronary calcium as a prognostic test: a Bayesian approach. Circ Cardiovasc Qual Outcomes. 2011;4:253-6. [PMID: 21406674] doi:10.1161/CIRCOUTCOMES.110.958496
7. **Nasir K, Bittencourt MS, Blaha MJ, Blankstein R, Agatson AS, Rivera JJ, et al.** Implications of coronary artery calcium testing among statin candidates according to American College of Cardiology/American Heart Association cholesterol management guidelines: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol. 2015;66:1657-68. [PMID: 26449135] doi:10.1016/j.jacc.2015.07.066
8. **Blaha MJ, Cainzos-Achirica M, Greenland P, McEvoy JW, Blankstein R, Budoff MJ, et al.** Role of coronary artery calcium score of zero and other negative risk markers for cardiovascular disease: the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation. 2016;133:849-58. [PMID: 26801055] doi:10.1161/CIRCULATIONAHA.115.018524
9. **Nasir K.** Message for 2018 cholesterol management guidelines update: time to accept the power of zero [Editorial]. J Am Coll Cardiol. 2018;72:3243-5. [PMID: 30409568] doi:10.1016/j.jacc.2018.10.006
10. **Roberts ET, Horne A, Martin SS, Blaha MJ, Blankstein R, Budoff MJ, et al.** Cost-effectiveness of coronary artery calcium testing for coronary heart and cardiovascular disease risk prediction to guide statin allocation: the Multi-Ethnic Study of Atherosclerosis (MESA). PLoS One. 2015;10:e0116377. [PMID: 25786208] doi:10.1371/journal.pone.0116377

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