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Coronary Artery Calcium Scoring in Current Clinical Practice: How to Define Its Value?

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Opinion statement

Detecting subclinical atherosclerosis with coronary artery calcium (CAC) is promising for identifying individuals at risk for cardiovascular events and appears to be a robust tool for guiding initiation of appropriate and timely primary prevention strategies. However, how do we best determine its clinical value? It is clear that traditional risk prediction models based primarily on age, gender, and risk factors are insufficient for ideal personalization of risk estimation. It is now well established from epidemiologic studies that CAC adds to traditional risk scores for a more accurate risk prediction. However, such traditional epidemiology studies have limitations in establishing "clinical value," and they must be supplemented by additional data before being translated into strong recommendations in clinical practice guidelines. Fortunately, over the last few years, the research around CAC has matured to include data supporting enhanced clinician-patient risk discussions, shared decision-making, flexible risk factor treatment goals, specific clinical decision algorithms, as well as favorable cost-effectiveness analyses. We had moved from a time

when we asked "if CAC adds to the risk score" to a time when we are asking "does CAC facilitate a shared decision-making model matching risk, treatment, and patient preferences?" A new risk calculator incorporating CAC into global risk scoring, and 2017 guidelines on the use of CAC published by the Society of Cardiovascular Computed Tomography (SCCT), reflect this new approach. In this article, we review the recent transition to this more clinically relevant CAC research that may support a stronger recommendation for its use in future prevention guidelines.

Introduction

Estimation of atherosclerotic cardiovascular disease (ASCVD) risk using the Pooled Cohort Equations (PCE) has been an important step towards identifying patients who might benefit from preventive pharmacotherapies. However, studies that have examined the PCE's risk calibration and discrimination have shown that it exhibits just moderate risk discrimination, and commonly overestimates ASCVD risk [1], perhaps because it uses one-time measures of risk factors derived from older cohorts that may not be fully representative of the current U.S. population [2]. This may be especially true among non-Caucasian and non-African American populations, and also among older populations since PCE is heavily weighted towards patient age [1, 3]. However, American College of Cardiology/American Heart Association (ACC/AHA) Guidelines offer recommendations for the use of supplementary tools, such as coronary artery calcium (CAC) scoring, for more accurate risk assessment beyond the PCE "when risk or the decision to treat is uncertain" [4–6]. This recommendation especially applies to patients determined to be at "intermediate" risk for ASCVD based on the traditional risk factor-based models [4, 7].

Head-to-head comparison of CAC with other novel biomarkers and traditional risk factors in the Multi-Ethnic Study of Atherosclerosis (MESA) has consistently shown that CAC is the single best prognosticator of the risk for coronary heart disease (CHD) [8•, 9••]. Similar results have been observed in the Heinz Nixdorf RECALL study [10] and in the Dallas Heart Study [11]. CAC scoring has been demonstrated to be helpful for reclassifying risk, statistically moving patients to lower or higher risk groups, and its preeminence for risk prediction was briefly noted in the 2013 ACC/AHA guidelines [4].

To further define the value of CAC score in terms of statistical risk prediction, the new MESA CHD Risk Score (developed in 2015) incorporates CAC—for the first time—into its equation [12••]. The addition of CAC score to MESA CHD risk score increased the risk discrimination significantly (area under the ROC curve for scores with and without CAC were 0.81 and 0.76, respectively), and it showed good calibration in two separate cohorts [7]. Although the MESA CHD risk score can discriminate risk and is well calibrated, the current version only predicts CHD, therefore, it cannot yet fully replace the PCE and is best used when ASCVD risk is intermediate [13].

The science of CAC has now extended from traditional risk prediction studies to patient-centered research with direct implications for personalized clinical practice. As current approaches for the prevention of ASCVD are explicitly risk-based, more endeavors have been required to understand how to convey CVD risk estimation and to use these approaches for shared decision-making [14]. Therefore, this review intends to articulate how CAC scoring has moved from purely epidemiologic inquiry (i.e., risk prediction studies) to innovative patient-centered science pointing at more routine clinical use to achieve improved outcomes. Herein, we summarize the novel research about CAC on clinician-patient risk discussions, shared decision-making, clinical decision tree algorithms and guidelines, selection of flexible risk factor treatment goals, and cost-effectiveness (Table 1).

Clinician-patient risk discussion

Recent prevention guidelines have placed emphasis on opening a discussion about the risk, potential benefits of treatments to reduce ASCVD risk, adverse effects of treatments, and drug-drug interactions, all in the context of patient preferences [16, 29]. The risk discussion is particularly pertinent for patients with

Table 1. Summary of recent studies on practical utility of CAC

	Author	Study	Important findings
Risk discussion	Gupta 2017 [15••]	Systematic review and meta-analysis	Nonzero CAC score significantly increases the likelihood of initiation or continuation of pharmacological and lifestyle therapies for the prevention of cardiovascular disease.
	Martin 2015 [16]	Review article	Risk discussion has a pivotal role in making a shared decision and includes benefits of reducing ASCVD, adverse effects of treatments, drug-drug interactions, and patient preferences.
	McClelland 2015 [12••]	MESA (MESA Risk Score)	CAC along with traditional risk factors can provide an accurate 10-year CHD risk estimate. MESA CHD Risk Score calculator can be used to guide risk-based treatment strategies.
Shared clinical decision-making	Hecht 2017 [17••]	Statement from the Society of Cardiovascular Computed Tomography	CAC scoring should be considered for patients with "intermediate" ASCVD risk. Potential harms from statin treatment or CAC scoring versus no treatment or no testing should be taken into account during shared decision-making.
	Nasir 2015 [18]	MESA	Among the patients considered for statin therapy according to the 2013 ACC/AHA guidelines, the absence of CAC reclassifies nearly 1 in 2 patients as not being eligible for statins.
	Mortensen 2016 [19•]	The BioImage Study	About 86% of participants in the study were eligible for statin therapy based on ACC/AHA guidelines with high sensitivity (96%) and low specificity (15%). Including CAC in risk prediction increases specificity by 22% without changing the sensitivity.
	Pursnani 2015 [20]	Framingham Heart Study	Participants who had CAC were more likely to be statin eligible by the 2013 ACC/AHA than by ATP III guidelines although many patients (63 vs 23%) with CAC = 0 were statin eligible.
	Blaha, 2016 [21••]	MESA	The absence of CAC resulted in the greatest downward shift in estimated CVD risk compared with negative results related to other 12 tested risk markers.
	Yeboah 2016 [8•]	MESA	CAC recommendations by the 2013 ACC/AHA identify a subgroup of the asymptomatic population with a calculated 10-year risk of $< 7.5\%$, but observed event rates $\geq 7.5\%$, who may benefit from statin therapy.
Flexibility of treatment goals	Blaha 2016 [22••]	Review article	A subgroup of patients with "advanced atherosclerosis" who might benefit from more intensive lipid-lowering therapy, as they are "between primary and secondary prevention."
	Miedema 2014 [23•]	MESA	Patients with CAC ≥ 100 had favorable net benefit with aspirin when used for primary prevention of

Table 1. (Continued)

	Author	Study	Important findings
			CHD, unlike those with CAC = 0 who were found to receive net harm from aspirin.
	McEvoy 2017 [24•]	MESA	Combined CAC and assessment of global ASCVD risk demonstrated promise in personalizing hypertension goals (choosing a traditional goal of 140 or an intensive target of 120 mm of Hg), particularly in those estimated to be at intermediate ASCVD risk, and pre-hypertension or mild hypertension.
Cost-effectiveness	Hong 2017 [25••]	MESA	CAC scoring showed similar clinical and economic consequences to treat all with statin strategy for intermediate-risk patients. The results support the role of shared decision-making according to patients preference and values.
	van Kempen 2016 [26]	FHS and Rotterdam Coronary Calcium study	CAC is cost-effective in men when there is disutility from taking long-term use, but not in women.
	Pletcher 2014 [27••]	MESA	Among adults with intermediate FRS risk, treating with statins among those with CAC > 0 was significantly more cost-effective than "treat-all" strategy only if statins are costly or significantly affect the quality of life.
	Roberts 2015 [28••]	MESA	Compared to alternative modalities that depend on traditional risk factors, CAC testing was found to be both effective and cost saving as a risk stratification tool especially for those with CAC ≥ 1 and CAC ≥ 100 when accounting for statin side effects and loss of quality of life.

ACC/AHA American College of Cardiology/American Heart Association, *ATP III* Adult Treatment Plan III, *ASCVD* atherosclerotic cardiovascular disease, *CHD* coronary heart disease, *FHS* Framingham Heart Study, *FRS* Framingham risk score, *LDL-C* low-density lipoprotein cholesterol, *MESA* Multi-Ethnic Study of Atherosclerosis, *JUPITER* Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin, *VADT* VA Diabetes Trial

"intermediate" CVD risk because appropriateness of, initiation of, and adherence to preventive treatment requires a more concrete understanding of risk [30, 31•]. CAC can further discriminate and contextualize risk in this setting to help guide preventive treatment strategies [32].

Direct visualization of disease using CAC scoring may provide a tangible, tractable understanding of ASCVD risk for individual patients, facilitating improved engagement in risk communication, and increase adherence to assigned preventive care [17••, 33]. A 2017 systematic review and meta-analysis by Gupta

et al. recently established that presence of CAC is independently associated with increase in physical activity, improved dietary changes, initiation of aspirin, and blood pressure medication as well as continuation of lipid-lowering medication [15••]. Patients tend to understand presence or absence of "disease" better than the statistics of risk. In this way, knowledge of CAC can foster informed decision-making helping a better adherence to more intensive lifestyle modifications and therapeutic interventions. For example, the presence of CAC in early adulthood, which signifies "early disease," has been shown to be associated with higher risk of CHD, CVD, and death [34]. Therefore, younger patients that are informed about their ASCVD risk status earlier in life may make life-saving decisions before asymptomatic subclinical ASCVD progresses to symptomatic clinical disease [35]. Patients otherwise considered low risk yet with elevated CAC, for example lower risk women, may be more thoroughly encouraged to engage in specific risk reducing behaviors beyond typical lifestyle recommendations given to all patients [36].

The 2013 ACC/AHA guideline placed an especial emphasis on allocation of statin therapy according to the PCE. In addition to patients with low-density lipoprotein cholesterol (LDL-C) level of 190 or higher, statin therapy is now indicated in patients with ASCVD risk of 7.5% or higher with the LDL-C level of 70–189. This pivot towards risk in statin indication makes the ASCVD risk assessment more important than ever [37]. CAC, which is recommended in patients with uncertain risk after PCE, may help the asymptomatic patients with modifiable risk factors like hypertension to understand that despite the optimal risk factor control they are still at higher risk of ASCVD compared to patients who do not have the risk factors. In this context, CAC is helpful because it can serve as a measure of biologic age—of accumulated disease—which is not modifiable, so it is different from traditional modifiable cardiovascular risk factors [38, 39]. So-called "disease scores" may be understood differently by patients as compared to risk factors [40], and thus might be useful aids in the clinician-patient risk discussion.

The interaction of CAC and potential benefit from preventive treatments gains additional meaning when placed in the critical context of the clinician-patient risk discussion [8•, 41••]. Previous studies have shown that CAC can effectively be used to communicate down-reclassification or up-reclassification of risk (as initially determined by Framingham Risk Score or 10-year ASCVD risk calculator) and concepts of net benefit [42–44]. For example, in an important recent paper by Yeboah et al., the presence of CAC was found to distinguish a greater risk for ASCVD meriting consideration for statins in a subgroup of participants with a 10-year ASCVD risk estimate < 7.5%. While a high CAC would suggest benefit with statin treatment, the absence of CAC may indicate low risk that may suggest little "net benefit" from statin treatment [45••]. Patients can typically understand that absence of CAC is associated with low ASCVD risk among those initially thought to be in low to intermediate risk. Similarly, among individuals considered to be at high risk by the more traditional clinical risk scores, a CAC score of zero also confers better survival than individuals at low to intermediate risk who have substantial CAC [46•]. Indeed, a recent study demonstrated that absence of CAC downgraded CVD risk the most when compared with other 12 negative risk markers [21••].

As previously mentioned, McClelland et al. introduced the MESA CHD Risk Score calculator in 2015 and validated this new score in independent

cohorts, including Heinz Nixdorf Recall (HNR) and Dallas Heart Study (DHS) [12••]. It is the first global risk score to incorporate the incremental predictive capability of CAC to refine risk prediction. It calculates risk by using CAC score in addition to demographic characteristics and traditional risk factors and reports estimated risk with and without considering CAC for each individual [12••]. The online MESA CHD Risk Score calculator (https://www.mesa-nhlbi.org/CAC-Tools.aspx) makes communication of results easier. Before ordering a CAC test, a physician can use this online tool to demonstrate to the patient how a theoretical CAC score might change the patient's risk. Then, after receiving a CAC result, the physician can again use the online calculator to demonstrate if the CAC test reclassified a patient's risk, or rather reinforced what was known about risk based on the risk factor profile. If the calculated risk with CAC is higher compared to when CAC was unknown, patients may decide to start preventive pharmacotherapy. On the contrary, lower CHD risk after factoring CAC in MESA CHD Risk Score compared to traditional risk factors alone may signal less net benefit from preventive therapy, thereby informing an interactive shared decision-making approach.

Shared decision-making

The 2013 ACC/AHA cholesterol guidelines [14] and the US Preventive Services Task Force (USPSTF) recommendations [47] are more patient-centered than prior guidelines, highlighting the importance of patients' preferences and values.

The recent 2017 statement from SCCT on the appropriate use of CAC testing stands out for placing CAC within this collaborative process between patients and health care professionals, providing "CAC based treatment recommendations within the context of the shared decision-making model espoused by the 2013 ACC/AHA Prevention guidelines." [17••] Health care professionals should ensure that patients are informed about all available options in the context of a risk-based approach [17••]. The shared decision-making process not only includes sharing the best available scientific evidence with patients (such as potential adverse effects of statins such as increased liver enzymes, myopathy, and increased risk of diabetes or the best tools for risk prediction [17••, 48]) but also takes into account patient's values and preferences [49]. In this context, an option that should be made available for select "intermediate-risk" patients who desire additional risk information is CAC scoring [17••]. Safety concerns regarding CAC scoring, such as its radiation exposure (approximately 1 mSv of radiation, equivalent to about two mammograms or two trans-Atlantic airplane flights) and implications of potential incidental pulmonary findings, versus benefits of more accurate risk stratification to start or defer lifelong statin therapy, should be part of the shared decision-making approach [17••].

Shared decision-making provides patients with the opportunity to weigh cons and pros of treatment with or without further testing and improves their awareness and engagement in disease management [18]. Here, a discussion is needed to help patients decide whether they wish to

(1) commit to lifelong treatment with statins if they fall under the rubric of any benefit groups without considering CAC results or (2) receive individualized treatment based on their CAC score [45••]. In an editorial, Hecht et al. [45••] proposed a wider role for CAC in shared decision-making. They argued that interested patients should be informed about both the limitations of traditional risk stratifying and the advantages of novel methods of risk estimation spearheaded by CAC scoring if more personalized care is one of the patient's stated goals. Although a large body of evidence supports the superior efficacy of CAC for improving risk stratification, patients should also be informed that future randomized controlled trials may be needed to test whether CAC-guided preventive treatments improve outcomes in real-world situations [50].

Therefore, patients are the principal decision makers who, armed with risk information and interpretation from their physicians, choose their intensity of treatment. The role of health care providers is presenting information to patients and harmonizing with patients' preferences [41••]. For example, a 50-year-old non-diabetic patient with an LDL-C = 130 and estimated 10-year ASCVD risk of 5.0% may seek further risk information and select CAC scanning. With CAC = 0, the patient may choose to be treated with statins regardless of their low-risk status, while others might defer treatment. In the latter case, the 2017 SCCT guidelines recommend repeating the CAC score in 5 years, with a repeat patient-physician discussion [46•].

Clinical decision and appropriate use algorithms

Recent research now suggests specific groups most likely to benefit from CAC, and this had led to the emergence of more specific clinical decision algorithms, for example, in the setting of treatment with statins. For example, Nasir et al. demonstrated that about 62% of MESA participants (age 59 ± 9 years; 53% females) were eligible (≥ 7.5%) or potentially eligible (≥ 5%) for statins based on their calculated 10-year estimated ASCVD risk using the PCE. Of these people, 44% had CAC = 0 and had consistently low observed 10-year incidence rate for ASCVD that downgraded their risk similar to that observed in the statin non-eligible group. The exception to this was in patients whose ASCVD risk was > 20%, as these individuals remained high risk regardless of CAC status. Among participants who were eligible or potentially eligible participants, the presence of any CAC was associated with a high incidence rate, resulting in these groups remaining statin eligible. Therefore, the absence or presence of CAC helps clinicians find more accurate statin benefit groups across each category of ASCVD risk [18]. Figure 1 illustrates a decision tree based on the presence or absence of CAC for patients with an ASCVD risk between 5–20%. Subsequent data from the Heinz Nixdorf RECALL study [51], the BioImage study [19•], and the Framingham Heart Study have led support to the general algorithm proposed by Nasir et al.

The 2017 statement from SCCT, which relied heavily on the evidence supplied by the Nasir et al. paper, provided two specific groups in whom CAC would be clinically appropriate:

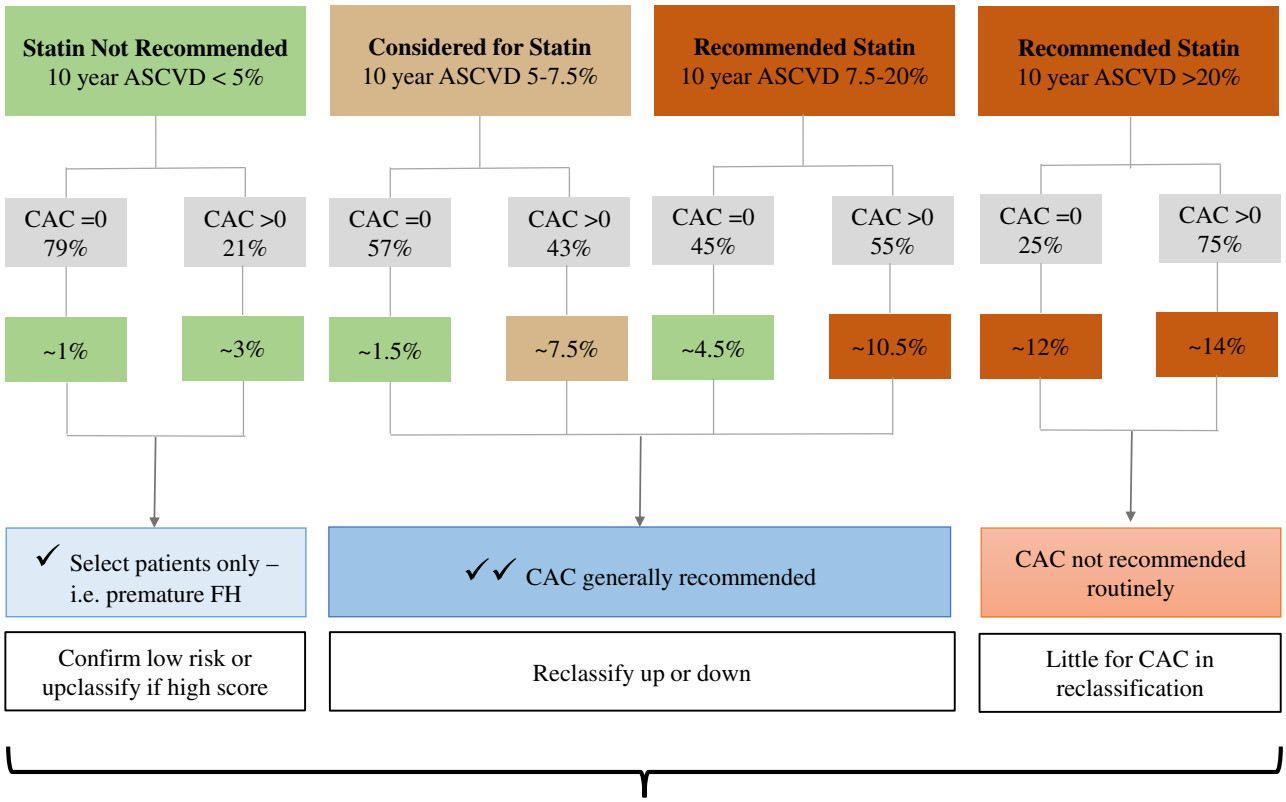

Fig. 1. Utility of CAC scoring for guiding statin therapy based on the 2017 SCCT CAC guidelines and Nasir et al. [18].

1. The most widespread application is likely to be in the 10-year ASCVD 5–15% risk group in which CAC = 0 and low CAC scores would largely refine risk downward to lowest or low strata, with treatment recommendations based on the score. In the 10-year ASCVD 15–20% risk group, downward risk reclassification may be considered with 0 or low CAC scores.
2. In the 10-year ASCVD < 5% risk group, for those patients who seek greater reassurance, e.g., young patients with a family history of premature CAD which does not factor into the PCE, a 0 or low CAC score would confirm their low-risk status and higher scores would identify those targeted for a greater intensity of lifestyle recommendations and treatment.

In these patients with ASCVD risk between 5 and 20%, or < 5% with a strong family history of the premature coronary disease, the SCCT has suggested use and intensity of statin treatment based on categories of CAC [32]. High-intensity statin treatment is recommended for patients with CAC ≥ 300 or above the 75th percentile for age/gender/race, consistent with the 2013 ACC/AHA guidelines. Also, moderate-to-high is recommended for patients with CAC of 100–299. For patients with CAC score between 1 and 99, moderate-to-high and moderate intensity statins are recommended for those with CAC percentile ≥75th and <75th, respectively. When CAC = 0, statins could be deferred based on patient preferences.

Flexible risk factor treatment goals guiding intensity of preventive pharmacotherapy

Guidelines are increasingly using risk to justify the selection of preventive medication intensity. CAC may have a role in individualizing CVD risk and providing flexible risk factor treatment goals for utilization and intensity of medications [8•, 18, 20, 43, 51]. Absence of CAC may loosen thresholds for preventive pharmacological treatment [52] and even excluding participants from preventive pharmacotherapy [18, 20, 44, 51]whereas high CAC may argue for the most aggressive treatment.

Lipid-lowering therapy

Patients with very high CAC (i.e., >90th percentile or >300 Agatston score) have been shown to have event rates comparable to "stable" secondary prevention patients. These high-risk patients are between primary and secondary prevention, given the abundance of asymptomatic coronary atherosclerosis without yet sustaining a coronary event [22••]. As a result, some of the results from secondary prevention trials might be pertinent to patients with abundant subclinical atherosclerosis who have not experienced CVD yet. For example, the recent IMPROVE-IT trial demonstrated that the decrease in LDL-C by statins, non-statin medications, or combination therapy would result in greater reduction in CVD risk after acute coronary syndrome [53, 54]. The FOURIER trial demonstrated that combination of a PCSK-9 inhibitor on a background of statin decreased the LDL-C to a median of 30 mg/dL and significantly reduced CVD risk by 15–20% after a median of 2.2-year treatment in patients with ASCVD [55]. Therefore, the benefits of intensive therapy for a lower LDL-C treatment goal (i.e., <70 mg/dL) may outweigh its harms among patients with very high CAC, while it might be reassuring to be less aggressive in those with average LDL-C levels and a CAC = 0 [32, 34, 35, 37]. As a result, CAC may guide flexible LDL-C treatment goals as a function of estimated risk.

Aspirin

Knowledge of CAC scores may help physicians and patients in making personalized risk-based therapeutic strategies such as aspirin and blood pressure medication intensity. Individuals with high CAC (generally > 100 Agatston score) seem to have a favorable risk-benefit estimation for aspirin use while those with no CAC would be unlikely to benefit from treatment. Indeed, in a modeling study using MESA data, Miedema et al. showed that participants with CAC ≥ 100 had favorable net benefit with aspirin treatment for CHD prevention. The 5-year NNT was estimated by using a median 7.6-year follow-up and applying 18% relative CHD reduction to the observed event rates. The 5-year number needed to harm was set to 422 for a major bleed according to an aspirin meta-analysis. A net benefit was found for individuals with CAC ≥ 100 (estimated NNT 173 for Framingham Risk Score (FRS) < 10% and 92 for individuals with

FRS ≥ 10%) while individuals with CAC < 100 was found to have lower NNTs (2036 if FRS < 10% and 808 for individuals with FRS ≥ 10%) [23•]. This is of particular importance as many patients with "intermediate" risk, who might have been prescribed aspirin for prevention, could perhaps safely avoid it if they had no CAC. Indeed, the 2017 statement published jointly by the Society of Cardiovascular Computed Tomography (SCCT) has suggested aspirin therapy for patients with CAC ≥ 100, because for lower CAC scores, the harms from gastrointestinal bleeding outweigh the benefits of aspirin treatment [17••].

Blood pressure

Prior studies have shown the role of CAC for suggesting risk-based blood pressure targets. McEvoy et al. showed that global ASCVD risk assessment, when combined with CAC, demonstrated promise in personalizing hypertension goals, particularly in those with systolic blood pressure < 160 mmHg and an estimated 10-year ASCVD risk between 5 and 15%. Using the observational data and estimated treatment effects, participants were predicted to have a lower (more favorable) NNT for a systolic blood pressure goal of ~ 120 mmHg with high CAC, for example > 100 [24•]. On the other hand, intensive treatment may have no net benefit for lower risk individual with CAC = 0, who might be managed with a traditional goal of 140 mmHg [32].

Based on the recently published papers, Table 2 presents a speculative approach for future treatment goals of risk factors according to CAC categories. This future-thinking approach provides a potential algorithm for clinicians to manage CVD risk beyond current guidelines recommendations. While optimal control of risk factors is crucial for better cardiovascular outcomes, this CAC-based strategy determines which patients would benefit from more intensive lifestyle modification, statin and aspirin therapy, and blood pressure lowering medications.

Table 2. Potential future flexible risk factor treatment goals based on categories of coronary artery calcium (CAC) for intermediate-risk patients

CAC score (Agatston)	Lifestyle modification	Statin use and intensity	Non-statin add-on therapy[a]	Aspirin	Blood pressure goal
0	√				
1–99					
< 75th %[b]	√	Moderate			Routine
≥ 75th %[b]	√	Moderate to high			Routine
100–299	√	Moderate to high		√	Routine
≥ 90th %	√√	High	Consider	√	Aggressive
≥ 300	√	High	Consider	√	Aggressive

[a]To achieve a low-density lipoprotein cholesterol of < 70 mg/dL
[b]Age, sex, ethnicity-adjusted percentiles

Cost-effectiveness of risk estimation using CAC

While statins are beneficial in reducing the enormous financial burden on health care systems from preventable CVD [56], better identification of and targeting primary preventive therapies to those likely to sustained ASCVD events cost-effectiveness analyses are needed to weigh benefits and harms of strategies that lead to treating or not treating with preventive medications. Recent studies have assessed whether benefits of routine use of CAC scoring in select patients for more accurate risk stratification outweigh its financial costs including out-of-pocket costs and low-dose radiation exposure [53–56]. Pletcher et al. demonstrated that treat-all strategy for statins for 10,000 55-year-old women with 10 years CHD risk = 7.5% and stroke risk = 0.9% might prevent 43 myocardial infarction, cause 70 cases of myopathy, and add 1108 years to total life expectancy. CAC-guided statin treatment for 2400 women in the same risk category with CAC > 0 would add 501 life-years but cost $2.25 million and cause nine radiation-induced cancers. Authors showed that CAC screening is cost-effective (with less than $50,000 per quality-adjusted-life-year) compared with treat-all strategy among patients with intermediate-risk scenarios who have a CHD risk between 5–10% if statins are expensive or if disutility is considered. Disutility refers to a preference to defer medical therapy in general, i.e., where a patient would be willing to trade 2 weeks of perfect health to avoid 10 years of statin treatment [27••].

Roberts et al. conducted further analyses by clinical and economic outcomes using different strategies regarding statin treatment among statin-naïve intermediate-risk participants with Adult Treatment Plan III (ATP III) Framingham Risk Score of 6–20% who had an LDL-C < 160 mg/dL. Authors demonstrated that CAC-guided treatments among participants with CAC > 0 are more cost-effective compared with treat-all strategy recommended by Adult Treatment Plan III (ATP III) guidelines if the CAC scoring is priced less than $235. Markov models also showed that treating patients with CAC ≥ 100 is cost-effective compared to existing guidelines if annual cost of statin therapy is higher than $1000 with additional consideration of a modest disutility from statin use [28••].

Most importantly, a new 2017 cost-effectiveness analysis by Hong et al. compared both the economic and clinical consequences of treat-all strategy in patients with intermediate risk with the utilization of CAC to guide long-term statin therapy using a microsimulation model with a societal perspective and lifetime horizon. In the base model analysis, they considered the direct and indirect costs of CAC scoring to be $215 and the annual cost of statin therapy to be $85. Economic and clinical consequences of two strategies were close. The CAC scoring approach resulted in $11,579 of cost and QALYs of 11.859, while the treat-all strategy cost $11,498 with a 1.849 QALYs. Similar economic and clinical consequences point specifically to accounting for individual preference in shared decision-making [25••]. Therefore, the clinician should take each patient's preferences and values into account when offering statins or CAC scoring to facilitate a shared decision-making approach.

Conclusion

Previous studies have demonstrated the superiority of CAC for predicting the risk of CVD, yet only recently have publications begun to reach beyond basic risk prediction to try to establish the clinical value of CAC. CAC appears to be a valuable part of clinician-patient risk discussion and shared decision-making. A recent meta-analysis has demonstrated that CAC significantly increases the likelihood of initiation or continuation of pharmacological and lifestyle therapies. Now, the MESA CHD Risk Score calculator can play a pivotal role in the translation of statistical findings related to CAC into useful clinical displays facilitating shared informed decisions by physicians and patients. Presence or absence of CAC among intermediate-risk patients (with a 10-year ASCVD risk score of 5–20%) re-stratifies their risk and yields easy-to-follow decision algorithms, for example, guiding statin and aspirin therapy. CAC has been shown to be a potentially cost-effective risk-stratifying tool among intermediate-risk patients by focusing treatment on those most likely to receive a net benefit. The 2017 SCCT guidelines have recognized a wider role for CAC, placing it specifically in the context of shared decision-making. We anticipate future guidelines to leverage recent results suggesting that CAC might be used to create flexible goals for treating risk factors such as LDL and systolic blood pressure [32].

Compliance with Ethical Standards

Conflict of Interest

Sina Kianoush, Mohammadhassan Mirbolouk, Raghavendra charan Makam, and Khurram Nasir each declare no potential conflicts of interest.

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Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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