

Coronary artery calcification in clinical practice: what we have learned and why should it routinely be reported on chest CT?

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Abstract: The recent acceptance of low dose chest computed tomography (LDCT) as a screening modality for early lung cancer detection will significantly increase the number of LDCT among high risk population. The target subjects are at the same time at high risk to develop cardiovascular (CV) events. The routine report on coronary artery calcification (CAC) will therefore, enhances the screening benefit by providing the clinicians with an additive powerful risk stratification tool for the management or primary prevention of CV events. This review will provide the radiologists with helpful information for the daily practice regarding on what is CAC, its clinical applications and how to diagnose, quantify and report on CAC while reading the LDCT.

Keywords: Atherosclerosis (AS); coronary artery calcification (CAC); risk prediction; chest computed tomography (chest CT)

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Introduction

CAC is a surrogate marker of the total burden of coronary atherosclerosis (AS). Its presence in asymptomatic subjects indicates the existence of subclinical coronary artery disease (CAD) and its quantity reflects the extent and the chronicity of the disease in the vessel wall. CAC can be easily detected and quantified from each low dose chest computed tomography (LDCT) that is clinically recommended. In 2010, CAC assessment was incorporated into American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines with a class IIa status (recommendation in favour of treatment or procedure being useful/effective). Measurement of CAC was considered reasonable for cardiovascular (CV) risk assessment in asymptomatic adults at intermediate risk, and all diabetic patients 40 years or older (1).

The American College of Cardiology Foundation (ACCF)/Society of Cardiovascular Computed Tomography (SCCT)/ACR(American College of Rheumatology)/AHA/ASE/American Society of Nuclear Cardiology (ASNC)/North American Society of Cardiovascular Imaging (NASCI)/SCAI/Society for Cardiovascular Magnetic Resonance (SCMR) 2010

use criteria deemed CAC appropriate for intermediate-risk patients as well as for low-risk individuals with a family history of premature disease (2). In 2012, the European Society of Cardiology awarded a similar class IIa recommendation, and suggested CAC for CV risk assessment in asymptomatic adults at moderate risk (3).

The recent acceptance of LDCT as a screening modality for early lung cancer detection by the National Comprehensive Cancer Network (4), the American College of Chest Physicians and the American Society for Clinical Oncology (5), the American Cancer Society (6), the American Association for Thoracic Surgery and the Society of Thoracic Surgeons (7), and the American Lung Association (8) will significantly increase the number of LDCT among high risk population. The target population of the screening program mainly, subjects above 55 years, current or ex-smokers are at the same time at high risk to develop CV events. The routine report on CAC will therefore enhances the screening benefit by providing the clinicians, cardiologist as general practitioners, with an additive powerful risk stratification tool for the management of primary prevention of CV events (9). Patients who meet

both CAC and lung scan criteria or lung scan criteria alone should be eligible for a combined full chest low-dose-gated computed tomography (CT) scan. The estimated 7,000,000 patients in the USA who fulfil lung screening criteria by United States Preventive Service Task Force (USPSTF) (10) are also at least intermediate risk for cardiac events because of their advanced age and long-standing smoking history, and will therefore be candidates for both evaluations.

This review will summarize the clinically applicable knowledge from more than three decades of intensive research in this field. I will focus on providing the radiologists with helpful information for the daily practice regarding on what is CAC, its clinical applications and how to diagnose, quantify and report on CAC while reading the LDCT.

What is coronary artery calcification (CAC)?

CAC is an unequivocal marker of intimal AS. It is the result of many complex biologic processes including genetic, risk factors and protective factors as well as all the influence of the life time acquired diseases and environmental factors.

- CAC is a dominant component of the advanced chronic forms of AS;
- CAC is a surrogate marker of the total burden of coronary AS: for each quantity of CAC there is five times higher quantity of non-calcified soft plaques (11);
- The prevalence and quantity of CAC increase with age and accelerate in men over 50 and women over 60 years;
- CAC is the sole component of coronary AS that can be detected non-invasively and quantified by unenhanced chest CT;
- Analysis of lung scans for CAC seems appropriate and has the potential to be the standard of care (9,10).

What is the biologic role of CAC? Dose heavy CAC stabilize the AS plaques?

Some clinical observation studies suggest that CAC might be a part, or the result, of a chronic healing process of the inflamed atherosclerotic plaque that characterizes the acute stage of CAD. Recent studies using serial new intra vascular ultrasound (IVUS) techniques (12-14) support the understandings that CAC stabilizes the AS plaque and clinically characterizes the chronic manifestations of stable CAD (15). Furthermore, these studies could also demonstrate that treatment with high dose of statin is associated with

increased CAC content and plaque stabilization. This understanding had been recently further strengthened by a newer invasive modality the optical coherence tomography or “virtual histology”. Using this technique Mizukoshi *et al.* (16) investigated the characteristics of coronary calcium in acute myocardial infarction (AMI), unstable angina pectoris (UAP), and stable angina pectoris (SAP). That investigator evaluated calcium deposits in the culprit lesions (30-mm segment) using optical coherence tomography in 187 patients with AMI (n=44), UAP (n=73), or SAP (n=70) and found that the arc, area, and length of calcium were significantly smaller in those with AMI and UAP than with SAP. Furthermore, the number of spotty calcium deposits (with an arc of <90°) per patient was significantly larger in the AMI and UAP groups than in the SAP group. The number of large calcium deposits (with an arc of >90°) per patient was significantly lower in the AMI and UAP groups than in the SAP group. Plaque rupture frequency correlated positively with the number of spotty calcium deposits and inversely with the number of large calcium deposits. They concluded that calcium was very spotty and more superficial in the culprit lesions of AMI and UAP and that these characteristics of calcium might play an important role in the pathogenesis of plaque vulnerability. These findings had been previously confirmed by using the first generation of spiral technique and the nongated dual spiral CT (17,18). Shemesh *et al.* (19) evaluated the coronary calcium patterns in 149 patients: 47 with chronic stable angina (SAP) compared with 102 patients surviving a first AMI. Prevalence of CAC was 81% among the AMI patients and 100% in the stable angina patients. The 547 calcific lesions identified in the AMI patients and the 1,242 lesions in the stable angina patients were categorized into three groups according to their extent: mild, intermediate, and extensive. The age-adjusted proportions of the highest level of calcification among AMI versus stable angina patients were: mild 18% *vs.* 3%, intermediate 49% *vs.* 18%, and extensive lesions 33% *vs.* 79%, respectively. In the AMI group 73 culprit arteries were identified: 16 (22%) had no calcium detected, whereas 30 (41%) had mild lesions, 20 (27%) had intermediate forms, and only 7 (10%) had extensive lesions. The conclusion from that study, similar to that of Mizukoshi *et al.* (16), was that extensive calcium characterizes the coronary arteries of patients with chronic stable angina, whereas a first AMI most often occurs in mildly calcified or non-calcified culprit arteries. This observation was also confirmed in a prospective outcome studies among high risk hypertensive patients (20,21) and among adults free of clinical CHD in the Multi-Ethnic Study of Atherosclerosis

(MESA) (22). Coylewright *et al.* reported on a comparison of CHD risk factors and event rates between participants with very high CAC ($n=257$) and high CAC ($n=420$). CAC was measured at baseline, and participants were followed for a median of 68 months. Very high CAC ($\geq 1,000$), compared to high CAC (400–999), was associated with male gender and older age. Those with very high CAC were more likely to develop angina, but not more likely to experience myocardial infarction, resuscitated cardiac arrest, or CHD death compared to high CAC. Total CHD event rates were greater for very high CAC (3.7 per 100 person-years) compared to high CAC (2.6 per 100 person-years). They concluded that both high and very high CAC are associated with an elevated risk of CHD events in those without symptomatic CHD at baseline; however, very high CAC is associated with an increased risk of angina, but not CHD death or MI, compared to high CAC. Recently that observation was confirmed in another prospective study (23) that followed 667 patients who underwent CT for CAC measuring and who were yearly evaluated during a mean follow-up period of 6.3 ± 3.4 years. That study demonstrated that subjects with extensive CAC are not firstly manifested as acute coronary events but presented a high level of chronic CAD-related events. In contrast, first acute CAD-related events occurred mostly in subjects with mild and moderate CAC score.

These data support the understanding that CAC might be a part of healing process which stabilizes the AS plaques.

CAC in primary prevention

The most important clinical value of CAC score is the diagnosis of early subclinical CAD. This contributes to more appropriate selection of those who are at the highest risk of future CV events and mortality for intensive preventive efforts. The superiority of CAC score over the classical and novel RF has been demonstrated in different populations with several prospective population studies (24–28). Furthermore, CAC measurement reclassify high risk groups such as diabetic (29–33), hypertensives (21,34–36), elderly (37) and smokers (38,39). Equally important is the absence of CAC which indicates an excellent prognosis in asymptomatic as well in the high risk groups (40–42). Recently Valenti *et al.* reported that a CAC score of 0 confers a 15-year warranty period against mortality in individuals at low to intermediate risk that is unaffected by age or sex. Furthermore, they found that in individuals considered at high risk by clinical risk scores, a CAC score of 0 confers better survival than in individuals at low to

intermediate risk but with any CAC score (42).

The RECALL study: Heinz Nixdorf Risk Factors Evaluation of Coronary Calcium and Lifestyle (43) study included 4,487 subjects without known CAD, ranging in age from 45 to 75 years, half of whom were women. The participants were placed into risk categories on the basis of standard CV risk factors, as defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines. Of the 4,137 participants with complete follow-up data, 93 suffered cardiac death or nonfatal MI—the primary end point. CAC scores in the highest quartile were compared with those in the lowest: the relative risk of a cardiac event when adjusted for NCEP ATP III category was—2.12 for women and 9.48 for men. Adding CAC scores to the FRS improved the area under the curve from 0.681 to 0.749 ($P < 0.003$) and to the National Cholesterol Education Panel ATP III categories from 0.653 to 0.755.

The Rotterdam study (37) showed that CACS improves classification of coronary heart disease (CHD) risk in the elderly. It demonstrated that in a general population of elderly patients at intermediate CHD risk, CAC scoring is a powerful method to reclassify persons into more appropriate risk categories. The study comprised 2,028 asymptomatic participants (age 69.6 ± 6.2 years) from the Rotterdam Study. During a median follow-up of 9.2 years, 135 hard coronary events occurred. Persons were classified into low ($< 10\%$), intermediate (10% to 20%), and high ($> 20\%$) 10-year coronary risk categories based on a Framingham refitted risk model. Reclassification by means of CAC scoring was most substantial in persons initially classified as intermediate risk. In this group, 52% of men and women were reclassified, all into more accurate risk categories.

The BioImage study (a clinical study of burden of atherosclerotic disease in an at-risk population): prevalence, impact, and predictive value of detecting subclinical coronary and carotid AS in asymptomatic adults (44). That study demonstrated that detection of subclinical carotid or coronary AS improves risk predictions and reclassification compared with conventional risk factors. A total of 5,808 asymptomatic U.S. adults (mean age: 69 years, 56.5% female) were enrolled. All patients were evaluated by CAC and novel 3-dimensional carotid ultrasound. Plaque areas from both carotid arteries were summed as the carotid plaque burden. The primary endpoint was the composite of CV death, myocardial infarction, and ischemic stroke. Broader secondary endpoint also included all-cause death, unstable angina, and coronary revascularization. Over a

median follow-up of 2.7 years, major events occurred in 216 patients (4.2%), of which 82 (1.5%) were primary events. Net reclassification significantly improved with either carotid plaque burden (0.23) or CAC (0.25). Events rates simultaneously increased with higher levels of both.

The MESA study (45): coronary calcium as a predictor of coronary events in four racial or ethnic groups. That study demonstrated that CAC score is a strong predictor of incident CHD and provides predictive information beyond that provided by standard risk factors in four major racial and ethnic groups in the United States. No major differences among racial and ethnic groups in the predictive value of calcium scores were detected. Data on risk factors were collected and scanning for CAC score had been performed in a population-based sample of 6,722 men and women, of whom 38.6% were white, 27.6% were black, 21.9% were Hispanic, and 11.9% were Chinese. Participants had no clinical CV disease at entry and were followed for a median of 3.8 years. There were 162 coronary events, of which 89 were major events (myocardial infarction or death from CHD). In comparison with participants with no CAC, the adjusted risk of a coronary event was increased by a factor of 7.73 among participants with coronary calcium scores between 101 and 300 and by a factor of 9.67 among participants with scores above 300. The areas under the receiver-operating-characteristic curves for the prediction of both major coronary events and any coronary event were higher when the calcium score was added to the standard risk factors.

In another analysis of the MESA study (46) the prognostic value of CAC score was compared to 5 novel risk markers; carotid intima-media thickness, ankle-brachial index, brachial flow-mediated dilation, high-sensitivity C reactive protein (CRP) as well as to the presence of family history of CHD for improvement in CV risk assessment in intermediate-risk participant without diabetes mellitus. After 7.6-year median follow-up, 94 CHD and 123 CVD events occurred. Addition of CAC, afforded the highest improved AUC (0.623 vs. 0.784) to the Framingham risk stratification while brachial flow-mediated dilation had the least (0.623 vs. 0.639). For incident CHD, the net reclassification improvement with CAC was 0.659 by far higher than brachial flow-mediated dilation (0.024), ankle-brachial index (0.036), carotid intima-media thickness (0.102), family history (0.160) and high-sensitivity CRP (0.079). Similar results were obtained for incident CVD.

Recently, the researchers of the MESA trial suggested a novel risk score to estimate 10-year CHD risk using CAC

and traditional risk factors based on the MESA data with validation in the HNR (Heinz Nixdorf Recall) study and the Dallas Heart Study (47). The Inclusion of CAC in the MESA risk score offered significant improvements in risk prediction. External validation in both the HNR and Dallas Heart Study studies provided evidence of very good discrimination and calibration. Additionally, the difference in estimated 10-year risk between events and nonevents was approximately 8% to 9%, indicating excellent discrimination. They concluded that the MESA risk score, can be easily used to aid clinicians when communicating risk to patients and when determining risk-based treatment strategies. This score is available online on the MESA web site.

Techniques and protocols

CAC categorization is the goal rather than score

There is a wide agreement on the ability to categorized CAC from LDCT into the four classic categories of the measured Agatston CAC score. It seems that this clinically important categorization into none, mild, moderate or severe calcifications can be obtained by all the currently available CT devices and by different protocols; ECG gated or un-gated; prospective or retrospective ECG triggering, using low mAs all achieving high concordance with the Agatston score categories. Recently the visual categorization of CAC into the four categories has been confirmed by a large study (48) that compared three scoring methods: overall visual assessment, segmented vessel-specific scoring, and Agatston scoring. By using low-dose CT performed for lung cancer screening in older, heavy smokers, that investigators could demonstrate that a simple visual assessment of CAC can be generated for risk assessment of CHD death and all-cause mortality, which is comparable to Agatston scoring and strongly associated with outcome.

Gated vs. ungated

The validation of Low-dose ungated MDCT for the presence of CAC and assessment of Agatston score is mostly important, as this technique should allow for atherosclerotic disease risk stratification among patients undergoing low-dose ungated lung CT evaluation without requiring additional scanning. This could be even better achieved due to the new multi-detector computed tomography (MDCT) scanners, with faster gantry rotation times, thinner slices

(detector row widths) and more detector rows. The faster gantry rotation times reduce susceptibility to cardiac motion, and thinner detector row widths allow for thinner slices and reduced partial volume effects, potentially making calcium measures more exact and reliable, even on studies obtained for other indications.

In a systematic review and meta-analysis by Xie *et al.* (49), found a strong agreement in CAC scores categorization between non-triggered CT and electrocardiography-triggered CT. Based on five studies (49-53) that authors concluded that compared with electrocardiography-triggered CT, a high calcium score category in nontriggered CT is a fairly reliable finding. However they found that nontriggered CT yielded false-negative score in 8.8% of individuals, and underestimated high score in 19.1%. Furthermore, based on these five studies comprising 34,028 asymptomatic participants, the authors could also conclude that in cardiac asymptomatic subjects mainly from lung cancer screening trials, increasing score categories in non-triggered CT were associated with increasing unadjusted and adjusted HR for CV death and with increasing risk of CV events.

Budoff *et al.* (50) evaluated the concordance of CAC scores on ungated (thoracic) and ECG-gated (cardiac) MDCT scans and found an excellent correlations between gated and ungated CAC ($r=0.96$). In that study categories of CAC were examined within commonly used clinical cut-points (0, 1-100, 101-400 and >400). Concordance was found in 47 (94%) of 50 cases, with three cases being overestimated by ungated studies. In another study of Wu *et al.* (51), studied the concordance of CAC scores on low-dose ungated (120 kVp, 20 mAs) and standard-dose ECG-gated MDCT (120 kVp, 150 mAs, retrospective ECG gating). They found five false-positive and five false-negative cases, compared to gated studies. All the miscategorized scores were 12 or less. The negative predictive values of CAC on low-dose in that study were 98% and 99% for observers 1 and 2, respectively. The inter-technique concordance of the four major score ranks (0, 1-100, 101-400, >400) was high ($\kappa=0.89$ for the two observers).

Low vs. standard dose

The accuracy of LDCT for CAC measurement and categorization had been validated in several studies (52-56). Kim *et al.* (52) have reported that, in comparisons of CAC between low radiation dose chest MDCT and ECG-triggered standard-dose CT, over 90% of patients with

CAC on ECG-triggered scans can be visualized on ungated CT. They further reported that application of a low milliamper-second setting of 30 mAs for coronary artery calcium detection and measurement from a retrospective reconstruction from low-dose chest CT images produces results that are well correlated with those obtained using dedicated calcium-scoring CT at 55 mAs. An additional finding is that the ECG-gating did not significantly affect the correlation of the results between prospective ECG-gated calcium-scoring CT and nongated low-dose chest CT with retrospective reconstruction. Shemesh *et al.* (55) assessed the coronary artery calcium measurement with two milliamper-second levels (55 and 165 mAs) using prospective ECG-gated MDCT. Those investigators calculated the calcium mass and calcium score in 51 asymptomatic participants by performing two consecutive CT examinations, the first with a setting of 165 mAs and the second with a setting of 55 mAs. The total calcium score between the high- and low-dose scans was well correlated with respect to the Agatston method and calcium mass ($r=0.97$, $P<0.001$ and $r=0.99$, $P<0.001$, respectively). A strong correlation was also found for each vessel. Jacobs *et al.* (56) found good interscan agreement of stratification of participants into Agatston score risk categories in low-dose ungated CT screening for lung cancer. The subjects in that study were 584 participants in the screening segment of a lung cancer screening trial that underwent two low-dose ungated MDCT examinations within 4 months (mean, 3.1 ± 0.6 months) of a baseline CT examination. Agatston score, volume score, and calcium mass score were measured by two observers. Interscan agreement of stratification of participants into four Agatston score risk categories (0, 1-100, 101-400, >400) was assessed. An Agatston score >0 was detected in 443 baseline CT examinations (75.8%). Interscan agreement of the four risk categories was good ($\kappa=0.67$). The Agatston scores were in the same risk category in both examinations in 440 cases (75.3%). They concluded that CV disease risk stratification with low-dose ungated MDCT is feasible and has good interscan agreement of stratification of participants into Agatston score risk categories.

Visual vs. dedicated Agatston score

The development of visual scores for CAC categorization is essential in order to provide the chest radiologist with a simple technique that is less time consuming than the Agtston score. At 2006, Shemesh *et al.* (57) suggested an

ordinal CAC score that was based on visual estimation of the extent of CAC in the territory of the main coronary arteries. Recently that group of investigators further validated the accuracy of this ordinal score by comparing it to the classical Agatston score using nongated low-dose CT scans, in 631 asymptomatic participants who had CT scans from 2010 to 2013. Their Ordinal and Agatston score were classified into categories. The Ordinal Score Categories showed excellent agreement [weighted kappa of 0.83; 95% confidence interval (CI): 0.79–0.88] with the Agatston score categories. They concluded that the use of the Ordinal score is readily obtained on low-dose CT scans that are used for CT screening for lung cancer and these scores are useful for risk stratification of CAD (58).

Jubal *et al.* (59) validated another visual scoring scheme compare against ECG-gated CT's and against the Shemesh visual scoring scheme (57) in a different cohort of lung cancer screening participants. Low and high mA nongated, gated and ECG-gated CT were compared with the Agatston score. They found that scores were highly correlated among readers, between the ECG-gated CT, non-gated high mA CT, non-gated low dose CT, and with the Agatston score. They also found an excellent correlation of visual scoring with Agatston scoring on ECG-gated and non-gated CT. They concluded that in lung cancer screening CT's both visual scoring correlated well with Agatston scores and with each other and that visual scoring might predict clinically significant CAC in major Agatston categories.

The study of Blair *et al.* (60) provides an additional support to the reliability of the ordinal score as an alternative to the Agatston score as well as to its predictive value for CV death. The investigators compared the ordinal and Agatston CAC scores and their relative association with CVD mortality in a nested case-control study of 4,544 consecutive community-living individuals undergoing “whole body” CT scans for preventive medicine. Cardiac gated 3 mm chest CTs and nongated 6 mm standard chest CTs were used. CVD death was recorded over 9 years follow-up. The intra- and inter-reader kappa for the ordinal CAC score was 0.90 and 0.76 respectively. The correlation of Agatston and ordinal CAC scores was 0.72 ($P < 0.001$). In models adjusted for traditional CVD risk factors, the odds of CVD death per 1 SD greater CAC was 1.66 (1.03–2.68) using the ordinal CAC score and 1.57 (1.00–2.46) using the Agatston score. They concluded that a simple ordinal CAC score is reproducible, strongly correlated with Agatston CAC scores and provides similar prediction for CVD death in

predominantly Caucasian community-living individuals. That study confirmed the results of Shemesh *et al.* (38) in a study of ungated thoracic CT scans performed for lung cancer screening in 8,782 smokers, with 72 month mean follow up. That study revealed significant ability of ungated studies to predict CV mortality. That authors found, that the rate of CV deaths increased with an increasing CAC score, using a simple ordinal system, categorizing scores from 0–12 based upon visual estimation per vessel. With use of subjects with an ordinal CAC score of 0 as the reference group, a CAC score of at least 4 was a significant predictor of CV death [odds ratio (OR), 4.7; 95% CI: 3.3–6.8; $P = 0.0001$]; when adjusted for sex, age, and pack-years of smoking, the ordinal CAC score remained significant (OR, 2.1; 95% CI: 1.4–3.1; $P = 0.0002$). They concluded that “visual assessment of CAC on low-dose CT scans provides clinically relevant quantitative information as to CV death”.

The predictive value of the visual score was further demonstrated by Vehmas *et al.* (61) who studied whether incidental visually detected chest atherosclerotic calcifications, which are unrelated to the indication of chest CT, predicts mortality. Five hundred and four men (aged 39–81 years, mean 63 years) who were screened for lung cancer with spiral CT and later visually scored for atherosclerotic calcifications in the aorta and the origin of its great branches plus in the coronary arteries 57 CV death were recorded at a mean follow-up time of 10.4 years. In that study calcifications in the left anterior descending artery (HR = 1.86, 1.29–2.67, $P = 0.001$) and brachiocephalic calcifications (HR = 1.65, 1.09–2.49, $P = 0.018$) predicted CV death. In accordance with the previously described studies, they concluded that incidental arterial calcifications in routine chest CT should be actively reported to aid the recognition, preventive measures and medication of early AS.

Jacobs *et al.* (62) confirmed that CAC can predict all-cause mortality and CV events on low-dose CT screening for lung cancer. That study was a case-cohort study and included 958 subjects 50 years old or older within the screen group of a randomized controlled lung cancer screening trial. During a median follow-up of 21.5 months, 56 deaths and 127 CV events occurred. Compared with a CAC score of 0, multivariate-adjusted HRs for all-cause mortality for CAC scores of 1–100, 101–1,000, and more than 1,000 were 3.00 (95% CI, 0.61–14.93), 6.13 (95% CI, 1.35–27.77), and 10.93 (95% CI, 2.36–50.60), respectively. Multivariate-adjusted HRs for coronary events were 1.38 (95% CI, 0.39–4.90), 3.04 (95% CI, 0.95–9.73), and 7.77 (95% CI,

2.44–24.75), respectively.

Practical comments for chest radiologists

These comments might be added to the report:

- The presence of CAC indicates worse CV prognosis;
- Intensive and comprehensive primary prevention should be taken including life style modification, and medical treatment according to the individual risk burden and diseases;
- Absence of CAC indicates excellent prognosis.

No CAC detected: visual score =0:

- Might be false negative: small calcific lesions are missed (Agatston score <10): the visual score is less sensitive in the younger group of <50 years and in women in whom small calcified plaques are more prevalent;
- More favorable prognosis for CV events;
- The presence of chronic obstructive CAD is very unlikely;
- Recommendations: Life style changes.

Mild CAC: visual score 1–4 (Agatston score 1–100):

- Mildly increased risk for CV event;
- Consider further coronary evaluation and primary preventive treatment according to the patient global risk;
- Life style changes should be more emphasized.

Moderate CAC: visual score 5–7 (Agatston score 101–400):

- Mildly increased risk of CV event;
- Consider further coronary evaluation and primary preventive treatment according to the patient global risk and clinical manifestations;
- In patients with Framingham risk intermediate and above ($\geq 10\%$ in 10 years) statin should be considered.

Severe CAC: visual score 8–12 (Agatston score >400):

- Mostly prevalent in old patients and in those with clinical CAD and or PVD;
- Significantly increases the CV risk and total mortality;
- In asymptomatic subjects consider further coronary evaluation by stress ECG, stress echo or SPECT imaging to R/O obstructive CAD;
- Statin therapy should be highly considered.

Summary

Routine reporting of the CAC score seen on nongated chest CTs could affect millions of people (10). From the

results of recent studies the American College of Chest Physicians, the American Society of Clinical Oncology, and the American Thoracic Society endorse annual screening for lung cancer with low-dose chest CT among adults following NSLT protocol: men and women 55 to 74 years of age who are currently smoking or who had quit smoking within the past 15 years with a ≥ 30 -pack-year history. It is estimated that 7 million Americans would be eligible for such a screening (10), a number that of course does not include the millions of additional adults who undergo a chest CT for other reasons. The strong association between smoking and CV risk, explains the high prevalence of CAC >0 that was over 50% in many of the studies (49), and the proportion of individuals with the highest category of CAC (similar to an Agatston score >400) that was approximately 20%.

It is estimated that more than half of US adults still do not have optimal levels of risk factors (63,64). Jacobs *et al.* (62) found that of adults referred for lung cancer screening >40% of those with a CAC score >1,000 were not taking antihypertensive or statin therapy, despite many having elevated blood pressure or cholesterol levels. Showing patients sample images from their scans will help to serve as a powerful visual tool to help motivate behavior change.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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