International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

The Role of Computed Tomography Cardiac Imaging in Risk Stratification of Coronary Artery Disease

Elsayed Hamed Zidan, Mohamed Ibrahim Amin, Hussam Ismael Ibrahim Ammar*, Basma Kamal Soliman

Radio-diagnosis Department, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author: Hussam Ismael Ibrahim Ammar**

Email: drhussamammar@gmail.com,

Abstract:

Coronary artery disease (CAD) remains one of the most important causes of morbidity and mortality worldwide, creating a continuous need for reliable tools that can accurately identify patients at increased cardiovascular risk. Although traditional clinical risk scores are widely used, they may be insufficient for detecting subclinical atherosclerosis or predicting future coronary events in some patients. Cardiac computed tomography has become an important non-invasive imaging modality for CAD evaluation, particularly through coronary computed tomography angiography (CCTA) and coronary artery calcium scoring (CACS). CCTA allows detailed anatomical assessment of coronary stenosis, plaque burden, plaque composition, and high-risk plaque features, while CACS provides a quantitative measure of calcified atherosclerotic burden and helps reclassify patients according to their actual cardiovascular risk. In addition, standardized systems such as CAD-RADS improve communication between radiologists and clinicians and guide appropriate management decisions. Recent advances, including functional CT assessment, perivascular fat attenuation index, radiomics, spectral CT, and machine learning, have further expanded the role of CT cardiac imaging in individualized risk stratification, early preventive intervention, and optimization of treatment strategies in patients with suspected or established CAD.

Keywords: Coronary artery disease; Cardiac computed tomography; Coronary CT angiography; Coronary artery calcium score; CAD-RADS; Risk stratification.

Introduction:

Since the CAD is considered the leading cause of death globally with a prevalence of 7% **(1)**, in addition to the significant morbidity that accounting for 182 million disability-adjusted life years in 2019. Hence, the need for adequate risk stratification tools facilitating better assessment of the risk of CAD, in order to introduce effective prevention measures and to optimize the treatment strategies **(2)**.

Historically, rapid access chest pain clinics used clinical history and examination followed by an exercise tolerance test to risk stratify patients presenting with chest pain caused by stable angina. This was generally followed by SPECT or invasive coronary angiography if warranted. Exercise tolerance testing has since been removed from guidelines because of its limited diagnostic sensitivity **(3).**

Recognizing the traditional risk factors associated with CAD has paved the way for the development of sophisticated scoring algorithms that effectively stratify patients by their risk of developing this condition. Several of these risk assessment tools have achieved significant clinical relevance and have been integrated in contemporary CVD prevention guidelines. Notably, the AHA endorses the use of the Framingham Coronary Heart Disease Risk Score (FRS) and the American College of Cardiology/AHA pooled cohort equation (ACC/AHA PCE) as the primary tools for assessing the risk of CVD incident. Similarly, the European Society of Cardiology advocates for the Systematic Coronary Risk Estimation 2 (SCORE2) as an essential tool for assessing comparable outcomes **(4).**

However, nowadays risk stratification for CAD remains a challenge, as traditional clinical risk scoring systems are often insufficient in identifying patients who continue to be at risk for coronary events. Recent clinical evidence emphasizes the critical role of cardiac imaging through CCTA in the management of patients with stable ischemic heart disease. Advanced computed tomography technology allows for precise quantification of plaque burden, identification of high-risk plaques, and functional assessments of coronary lesions to detect ischemia and guide revascularization efforts for patients suffering from refractory angina symptoms. Moreover, contemporary CT machines are enhanced by the Perivascular Fat Attenuation Index (FAI), a non-invasive measurement of coronary inflammation that facilitates the direct quantification of residual inflammatory burden on the vascular system. In addition, the integration of machine learning, radiomic feature extraction, and spectral CT for tissue characterization is expected to significantly enhance the diagnostic and prognostic efficacy of CCTA. By combining anatomical, functional, and biological insights into coronary circulation, CCTA provides a robust toolkit for more accurate risk stratification and aids in the identification of patients who may benefit from targeted and aggressive prevention strategies. This comprehensive approach not only elevates patient care standards but also contributes to the ongoing advancement of cardiovascular health **(5).**

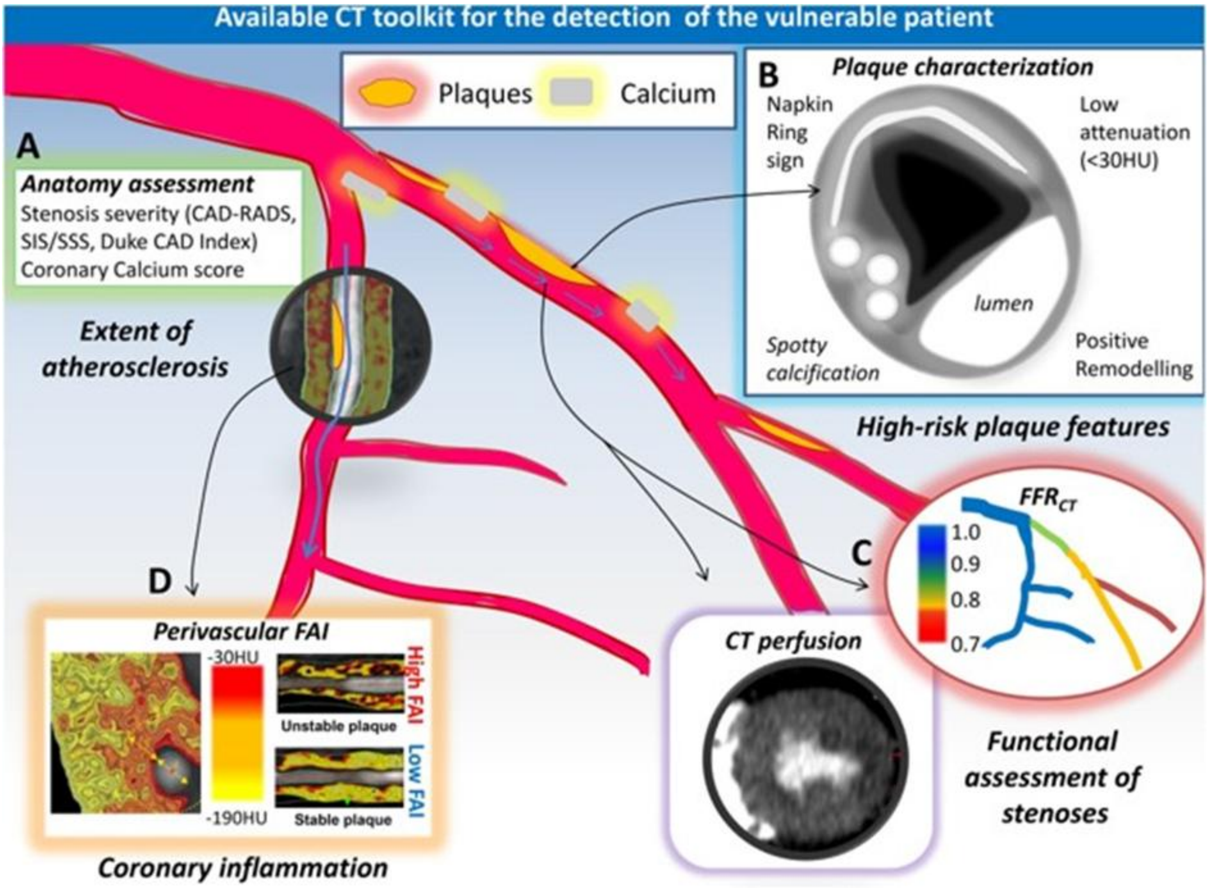

Figure 1. CT toolkit for the detection of the vulnerable patient **(6).**

It is worth mentioning here that CCTA is considered the backbone of the Coronary Artery Disease Reporting and Data System (CAD-RADS), first published in 2016 illustrated in (**table 1**), to standardize risk stratification and the reporting system for suspected CAD patients undergoing CCTA, and to guide possible next steps in patient management **(7).**

Table 1 CAD-RADS reporting and data system for patients presenting with stable chest pain **(8).**

CAD-RADS reporting and data system for patients presenting with stable chest pain.

	Degree of maximal coronary stenosis	Interpretation	Further Cardiac Investigation	Management
CAD-RADS 0	0% (No plaque or stenosis)	Documented absence of CAD[a]	None	- Reassurance. Consider non- atherosclerotic causes of chest pain
CAD-RADS 1	1–24% - Minimal stenosis or plaque with no stenosis[b]	Minimal non-obstructive CAD	None	- Consider non- atherosclerotic causes of chest pain - Consider preventive therapy and risk factor modification
CAD-RADS 2	25–49% Mild stenosis	Mild non-obstructive CAD	None	- Consider non- atherosclerotic causes of chest pain - Consider preventive therapy and risk factor modification, particularly for patients with non-obstructive plaque in multiple segments.
CAD-RADS 3	50–69% stenosis	Moderate stenosis	Consider functional assessment	- Consider symptom-guided anti-ischemic and preventive pharmacotherapy as well as risk factor modification per guideline-directed care[c] - Other treatments should be considered per guideline-directed care[c]
CAD-RADS 4	**A** - 70–99% stenosis or **B** - Left main >50% or 3- vessel obstructive (≥70%) disease	Severe stenosis	A: Consider ICA[d] or functional assessment B: ICA is recommended	- Consider symptom-guided anti-ischemic and preventive pharmacotherapy as well as risk factor modification per guideline-directed care[c] - Other treatments (including options of revascularization) should be considered per guideline-directed care[c]
CAD-RADS 5	100% (total occlusion)	Total coronary occlusion	Consider ICA and/or viability assessment	- Consider symptom-guided anti-ischemic and preventive pharmacotherapy as well as risk factors modification per guideline-directed care[c] - Other treatments (including options of revascularization) should be considered per guideline-directed care[c]
CAD-RADS N	Non-diagnostic study	Obstructive CAD cannot be excluded	Additional or alternative evaluation may be needed	

The CAD-RADS classification should be applied on a per-patient basis for the clinically most relevant (usually highest-grade) stenosis.
All vessels greater than 1.5 mm in diameter should be graded for stenosis severity. CAD-RADS will not apply for smaller vessels (<1.5 mm in diameter).
MODIFIERS: If more than one modifier is present, the symbol "/" (slash) should follow each modifier in the following order:
First: modifier N (non-diagnostic)
Second: modifier **S (stent)**
Third: modifier **G (graft)**
Fourth: modifier **V (vulnerability)**
[a] CAD – coronary artery disease
[b] CAD-RADS 1 – This category should also include the presence of plaque with positive remodeling and no evidence of stenosis
[c] Guideline-directed care per ACC Stable Ischemic Heart Disease Guidelines (Fihn et al. JACC 2012).[25]
[d] ICA – invasive coronary angiography.

Those patients with a very high-risk pre-test likelihood of coronary artery disease, the 2010 National Institute for Health and Care Excellence guidelines suggested performing no investigation and to treat it as angina. However, this may potentially be denying this group an assessment of their 'ischemia burden', a discriminator that is known to confer prognostic information (**9).** The CE-MARC 2 trial identified that the 2010 National Institute for Health and Care Excellence guidelines led to higher rates of unnecessary angiography compared to functional imaging-guided care; a strategy that potentially increases patient morbidity and healthcare costs **(10**).

Finally, radiological quantification of CAC is known as a relatively noninvasive modality that has been developed more recently. It is a powerful predictor of the presence of an underlying atherosclerotic burden and can be determined either by fast electron beam CT or multidetector CT. It gives information about coronary plaque burden and therefore permits to risk stratify patients. Its incremental benefit on CAD risk prediction beyond conventional risk factors also has been demonstrated in several studies. The CACS has an independent prediction of CAD that a higher score is accompanied with a greater likelihood of having CAD. An independent positive correlation has also been observed between CACS and other cardiovascular risk factors such as age, gender, DM, hypertension and dyslipidemia **(11).**

CACS is the most reliable means of identifying risk. For example, intermediate-risk patients without CAC can be reclassified into a lower-risk group, such that statins can be withheld **(12).**

CACS is quantified almost exclusively by electrocardiogram-gated multidetector CT scan **(Figure 2).** Depending on the number of CT detector rows, CACS data can be acquired in just a few heartbeats. The best-quality data are acquired during mid-diastole, when the cardiac cycle is most quiescent. With recent advances in CT technology and dose-reduction techniques, the CACS radiation dose can be relatively small (0.37 ± 0.16 mSv), slightly lower than screening mammography (0.44–0.56 mSv) (**13).**

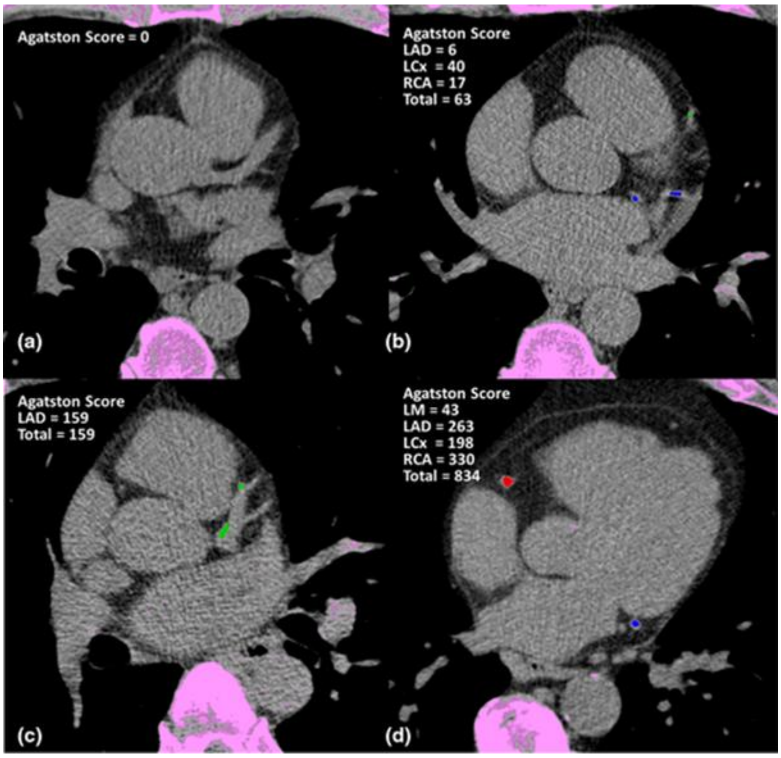

Figure 2. Representative examples of CAC in 4 patients. (A) A 52-year-old white man with no CAC. (B) A 64-year-old black man with CAC in the LAD (green) and LCx (blue); Agatston score = 63 (mild CAC), placing this patient within the 75th to 90th percentile for his age group. CAC was also present in the RCA (not shown). (C) A 50-year-old Asian man with CAC in the proximal, mid- and distal LAD (green); Agatston score = 159 (moderate CAC), placing this patient within the 90th to 95th percentile for his age group. CAC was also present in the distal LAD (not shown). (D) A 60-year-old white man with LM and 3-vessel CAC; Agatston score = 834 (severe CAC), placing this patient in the 95th percentile for his age group. CAC at only one level is shown: LCx (blue) and RCA (red). CAC, coronary artery 432calcification; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; LM, left main coronary artery; RCA, right coronary artery **(14).**

The **Agatston score (Table 2),** is the most widely used CAC scoring system in clinical practice and research. Total CACS is computed by summing the scores of all calcified lesions and can be expressed as a percentile, adjusted for sex and race (white, Chinese, black, Hispanic). CACS can also be computed for each coronary artery (**14).**

Table 2 Agatston score for coronary artery disease grading **(15).**

Maximum HU	Density factor	Agatston score	CAD grade
<147	0	0	No evidence of CAD
147–199	1	1–10	Minimal
200–299	2	11–100	Mild
300–399	3	101–400	Moderate
⩾400	4	>400	Severe

Moreover, CACS can be used in the assessment of plaque burden within the coronaries to predict the severity extent of CAD (**Table 3).** Subsequently, based on plaque burden provided by CACS, it is possible to consider a specific management plan to each patient corresponding to the CAD-RADS category **(Table 4).**

Table 3. Coronary plaque burden **(16).**

	Amount of plaque	Calcium score	SIS*	Visual
P1	Mild	1-100	≤2	1-2 vessels with mild amount of plaque
P2	Moderate	101-300	3-4	1-2 vessels with moderate amount; 3 vessels with mild amount of plaque
P3	Severe	301-999	5-7	3 vessels with moderate amount; 1 vessel with severe amount of plaque
P4	Extensive	>1000	≥8	2-3 vessels with severe amount of plaque

*SIS – Segment involvement score. SIS is a semiquantitative measure derived from the coronary CTA scan. For each of the 16 coronary segments a score o 1 is added if any plaque is present for a maximum of 16, or 17 in case a ramus intermedius is present.

Table 4. Management considerations based on plaque burden **(16).**

CAD-RADS1	Consider non-atherosclerotic causes P1: Consider risk factor modification and preventive pharmacotherapy P2: Risk factor modification and preventive pharmacotherapy P3/P4: Aggressive risk factor modification and preventive pharmacotherapy
CAD-RADS 2	Consider non-atherosclerotic causes P1/P2: Risk factor modification and preventive pharmacotherapy P3/P4: Aggressive risk factor modification and preventive pharmacotherapy
CAD-RADS 3	P1/P2/P3/P4: Aggressive risk factor modification and preventive pharmacotherapy Other treatments (including anti-anginal therapy) should be considered per guideline When modifier I+, consider ICA, especially if frequent symptoms persist after guideline-directed medical therapy
CAD-RADS 4A/B	P1/P2/P3/P4: Aggressive risk factor modification and preventive pharmacotherapy Other treatments (including anti-anginal therapy and options of revascularization) should be considered per guideline
CAD-RADS 5	P1/P2/P3/P4: Aggressive risk factor modification and preventive pharmacotherapy Other treatments (including anti-anginal therapy and options of revascularization) should be considered per guideline

One last CACS benefit as a powerful risk stratification tool is its ability to predict future risk of coronary events (myocardial infarction, death from coronary heart disease or resuscitated cardiac arrest) in asymptomatic patients, which is more accurate than clinical risk scoring alone, and in symptomatic patients it correlates positively with the degree of luminal obstruction of coronary artery **(17).**

References:

1. Tsao, C. W., Aday, A. W., Almarzooq, Z. I., Alonso, A., Beaton, A. Z., Bittencourt, M. S., Boehme, A. K., Buxton, A. E., Carson, A. P., Commodore-Mensah, Y., Elkind, M. S. V., Evenson, K. R., Eze-Nliam, C., Ferguson, J. F., Generoso, G., Ho, J. E., Kalani, R., Khan, S. S., Kissela, B. M., Knutson, K. L., … Martin, S. S. (2022). Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. Circulation, 145(8), e153–e639 .
2. Javed, Z., Haisum Maqsood, M., Yahya, T., Amin, Z., Acquah, I., Valero-Elizondo, J., Andrieni, J., Dubey, P., Jackson, R. K., Daffin, M. A., Cainzos-Achirica, M., Hyder, A. A., & Nasir, K. (2022). Race, Racism, and Cardiovascular Health: Applying a Social Determinants of Health Framework to Racial/Ethnic Disparities in Cardiovascular Disease. Circulation. Cardiovascular quality and outcomes, 15(1), e007917.
3. Knuuti J, Wijns W, Saraste A et al. ESC Guidelines for the diagnosis and management of chronic coronary syndromes The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC). Eur Heart J. 2020;41(3):407–477.
4. Antonopoulos, A. S., Angelopoulos, A., Tsioufis, K., Antoniades, C., & Tousoulis, D. (2022). Cardiovascular risk stratification by coronary computed tomography angiography imaging: current state-of-the-art. European journal of preventive cardiology, 29(4), 608–624.
5. Lopez-Jimenez, F., Almahmeed, W., Bays, H., Cuevas, A., Di Angelantonio, E., le Roux, C. W., ... & Wilding, J. P. (2022). Obesity and cardiovascular disease: mechanistic insights and management strategies. A joint position paper by the World Heart Federation and World Obesity Federation. European journal of preventive cardiology, 29(17), 2218-2237.
6. Cury RC, Leipsic J, Abbara S, Achenbach S, Berman D, Bittencourt M, et al. CAD-RADS™ 2.0 – 2022 Coronary Artery Disease – Reporting and Data System An Expert Consensus Document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Cardiology (ACC), the American College of Radiology (ACR) and the North America Society of Cardiovascular Imaging (NASCI). Radiology: Cardiothoracic Imaging. 2022;4(5):e220183.
7. Cury, R. C., Abbara, S., Achenbach, S., Agatston, A., Berman, D. S., Budoff, M. J., Dill, K. E., Jacobs, J. E., Maroules, C. D., Rubin, G. D., Rybicki, F. J., Schoepf, U. J., Shaw, L. J., Stillman, A. E., White, C. S., Woodard, P. K., & Leipsic, J. A. (2016). CAD-RADS(TM) Coronary Artery Disease - Reporting and Data System. An expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Radiology (ACR) and the North American Society for Cardiovascular Imaging (NASCI). Endorsed by the American College of Cardiology. Journal of cardiovascular computed tomography, 10(4), 269–281.
8. Nagel E, Shaw LJ. The assessment of ischaemic burden: thoughts on definition and quantification. Eur Heart J Cardiovasc Imag. 2014;15(6):610–611.
9. Walker S, Cox E, Rothwell B et al. Cost-effectiveness of cardiovascular imaging for stable coronary heart disease. Heart. 2021;107(5):381–388 .
10. Liaquat, A., Khan, A., Shah, S. U., Iqbal, H., Iqbal, S., Rana, A. I., & Rahman, H. U. (2022). Evaluating the use of coronary artery calcium scoring as a tool for coronary artery disease (CAD) risk stratification and its association with coronary stenosis and CAD risk factors: a single-centre, retrospective, cross-sectional study at a tertiary centre in Pakistan. BMJ open, 12(7), e057703.
11. Lloyd-Jones DM, Braun LT, Ndumele CE 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 2019; 73: 3153–67.
12. Hecht HS, de Siqueira ME, Cham M et al. Low- vs. standard-dose coronary artery calcium scanning. Eur Heart J Cardiovasc Imaging 2015; 16: 358–63.

13. Cheong BY, Wilson JM, Spann SJ, Pettigrew RI, Preventza OA, Muthupillai R. Coronary artery calcium scoring: an evidence-based guide for primary care physicians. Journal of Internal Medicine. 2021 Mar;289(3):309-24.
14. Brix, Mikael & Sepponen, Pasi & Korhonen, Kristiina & Pohjanen, Vesa-Matti & Ketola, Juuso & Kotiaho, Antti & Nieminen, Miika & Inkinen, Satu. (2020). Interior photon counting computed tomography for quantification of coronary artery calcium: pre-clinical phantom study. Biomedical Physics & Engineering Express. 6. 10.1088/2057-1976/aba133.
15. Celeng, C., Takx, R., Smithuis, R., & Leiner, T. (2023). Coronary artery disease reporting and data system (CAD-RADS). The Radiology Assistant. https://radiologyassistant.nl/cardiovascular/cad-rads/coronary-artery-disease-reporting-and-data-system#cad-rads-assessment-of-stenosis-degree.
16. Greenland, P., Blaha, M. J., Budoff, M. J., Erbel, R., & Watson, K. E. (2018). Coronary calcium score and cardiovascular risk. Journal of the American College of Cardiology, 72(4), 434-447.