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Review paper

Diagnostic and prognostic value of coronary artery calcium scoring and computed tomography angiography in coronary artery disease: a systematic review and meta-analysis

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Abstract

Coronary artery disease (CAD) remains a leading cause of disability and death worldwide. Noninvasive tests are crucial to ensure early diagnosis and risk stratification. The coronary artery calcium scoring (CACS), a non-invasive measure obtained using non-contrast computed tomography, reflects the calcific plaque burden, and may provide important diagnostic and prognostic information.

This study aimed to systematically review and meta-analyze the recent literature to ascertain the diagnostic and prognostic usefulness of CACS in patients with suspected or established CAD.

A literature search was conducted in PubMed, Scopus, and Web of Science for studies published between 2008 and 2024. The studies were included if they evaluated the prognostic and diagnostic value of CACS, either alone or with computed tomography angiography (CTA). Data extraction was performed for pooled sensitivities and specificities, hazard ratios (HRs), and event-free survival. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) criteria were used to assess methodological quality.

Fourteen high-quality studies with a total of more than 80,000 patients were meta-analyzed. Subjects with CAC ≥ 100 were at a significantly increased risk of developing major adverse cardiac events (HR 2.7; 95% confidence interval: 2.1-3.6). CACS is highly beneficial in diagnostic discrimination (pooled sensitivity 88%, specificity 77%) in those presenting with chest pain but no prior history of CAD. It is essential to emphasize that CAC score of zero correlates with the best prognosis and very low rates of clinical events across various populations, including patients with diabetes and asymptomatic individuals.

The CACS fills a special niche as a very strong predictor and non-invasive marker in the diagnosis and prognosis of CAD. Combining calcium scoring with CTA benefits clinical decision-making, particularly for patients categorized as low to intermediate risk.

Key words: coronary artery disease, coronary calcium scoring, computed tomography angiography, cardiovascular risk assessment, meta-analysis.

Introduction

The global burden of coronary artery disease (CAD) is increasing with the growth of aging populations and lifestyle risk factors such as diabetes, hypertension, smoking, and dyslipidemia, killing more than 9 million every year; it is the number one cause of death worldwide [1]. CAD is characterized by increased accumulation of atherosclerotic plaques in coronary arteries, leading to stenosis and ischemia and eventually myocardial infarction.

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Authors' contribution:

A Study design · **B** Data collection · **C** Statistical analysis · **D** Data interpretation · **E** Manuscript preparation · **F** Literature search · **G** Funds collection

Table 1. Comparison of traditional diagnostic tools and emerging imaging modalities in coronary artery disease evaluation

Modality	Sensitivity (%)	Specificity (%)	Invasiveness	Key limitations
ETT	~68	~77	Non-invasive	Low sensitivity in women and elderly; electrocardiography artifacts
MPI	~85	~75	Non-invasive	Radiation exposure; limited anatomical detail
MRI-MPI	~86	~83	Non-invasive	Limited availability; contraindicated in patients with implants; motion artifacts possible
Stress echocardiography	~80	~84	Non-invasive	Operator-dependent; image quality limitations
ICA	~95	~100	Invasive	Procedural risks; not suitable for all patients
CTA	~95	~90	Minimally invasive	May overestimate stenosis in calcified vessels
CACS	~80 (prognostic)	~70 (prognostic)	Non-invasive	Does not assess luminal narrowing; no information on soft plaques

CACS – coronary artery calcium scoring, CTA – computed tomographic angiography, ETT – exercise treadmill test, ICA – invasive coronary angiography, MPI – myocardial perfusion imaging, MRI-MPI – magnetic resonance imaging-myocardial perfusion imaging

Prompt detection of subclinical atherosclerosis and risk stratification are essential in managing guidelines for primary prevention and therapeutic intervention.

Classical CAD diagnostic methods include clinical risk scores, exercise treadmill testing (ETT), echocardiography, nuclear myocardial perfusion imaging (MPI), and invasive coronary angiography (ICA). Although ICA is considered the gold standard in anatomic assessment of coronary stenosis, it is confined to selected population groups due to being invasive, having complications, and high costs (Table 1). Noninvasive stress testing modalities, including ETT and MPI, show moderate sensitivity and specificity at best, especially in intermediate-risk populations.

The capabilities of coronary angiogram imaging have been greatly enhanced with the advent of computed tomography angiography (CTA). Coronary artery vessels can now be visualized at high resolution with intracardiac nonobstructive plaques. In addition, CTA enables assessment of coronary plaque composition and quantification of calcified and non-calcified plaque burden [2]. Multicenter trials such as PROMISE and SCOT-HEART have successfully demonstrated the clinical utility of CTA in improving diagnostic certainty, in management of patients, and, potentially, long-term clinical outcomes [3,4].

Along with CTA, coronary artery calcium scoring (CACS) has attracted great attention as it helps in risk stratification and early detection of coronary atherosclerosis through non-contrast computed tomography (CT) imaging. CACS provides a quantitative measure known as the coronary artery calcium (CAC) score. CAC score measures the total coronary plaque burden using the Agatston score and is well correlated with cardiovascular events [5]. When the CAC score is equal to zero, it is regarded as a low risk of future cardiac events and is increasingly used as a "gatekeeper" in deferring further tests [6]. In contrast, a higher calcium scores significantly increase the risk of myocardial infarction and mortality [7,8].

Multiple meta-analyses have verified prognostic implications of CACS. Lo-Kioeng-Shioe *et al.* [2] demonstrated that elevated CAC significantly predicted major adverse cardiovascular events (MACE), while Sarwar *et al.* [9] confirmed the strong negative predictive value of zero calcium. Further evidence from various studies supports CACS and CTA as synergistic methods to improve diagnostic accuracy and stratify patients with suspected CAD.

Despite its importance as a prognostic tool, CACS has not found universal application in clinical practice because of variability in guidelines, concerns over cost-effectiveness, and radiation exposure. Nevertheless, with advancements in the field of CT technology and dose reduction techniques, the risk-benefit ratio is getting better for CACS. As evidence accumulates, major guidelines issued by the American College of Cardiology and the European Society of Cardiology increasingly recognize the use of calcium scoring for selected patient groups.

In keeping with the more fluid roles that CACS is assuming in today's cardiovascular diagnostics, this systematic review and meta-analysis aims to comprehensively assess the diagnostic and prognostic performance of CACS in patients with suspected or known CAD. Specifically, the utility of CACS across different clinical presentations, populations, and in conjunction with CTA will be examined so that the current and possible future clinical application of CACS can be further elucidated.

Material and methods

Search strategy

This systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Exhaustive literature searches were carried out on the databases of PubMed, Scopus, and Web of Science searching for any relevant study published from January 2008 to April 2024.

Table 2. Characteristics of included studies

Author/year	Country	Sample size	Population type	Imaging method	Follow-up period	Outcomes measured
Chaikriangkrai *et al.*, 2016 [1]	USA	3,063	Symptomatic	CACS + CTA	3 years	MACE, all-cause mortality
Lo-Kioeng-Shioe *et al.*, 2020 [2]	Multi-national	34,000	Symptomatic	CACS	5 years	MACE, CAD-related mortality
Koopman *et al.*, 2022 [3]	Netherlands	1,200	Stable chest pain	CACS + CTA	2 years	Obstructive CAD, hospitalization
Tramontano *et al.*, 2022 [4]	Italy	5,216	Asymptomatic	CACS	4.5 years	Cardiovascular events, death
Sarwar *et al.*, 2009 [9]	USA	27,125	Mixed (symptomatic + asymptomatic)	CACS	5 years	Prognosis with CAC = 0
den Dekker *et al.*, 2012 [10]	Netherlands	1,408	Symptomatic	CTA stratified by CACS	3 years	Diagnostic accuracy based on CAC levels
Kramer *et al.*, 2013 [11]	Canada	6,521	Diabetic patients	CACS	5 years	All-cause mortality, cardiovascular events
Agha *et al.*, 2022 [12]	USA	3,210	Chest pain (low-risk)	CACS	2-4 years	Prognostic value of CAC = 0

CAC – coronary artery calcium, CACS – CAC scoring, CAD – coronary artery disease, CTA – computed tomography angiography, MACE – major adverse cardiovascular events

The search terms consisted of combinations of "coronary artery calcium," "CAC score," "computed tomography," "cardiac CT," "CTA," "coronary artery disease," "diagnosis," and "prognosis." Boolean operators and Medical Subject Headings were used to narrow down the search.

Inclusion and exclusion criteria

Eligible studies met the following criteria:
- original research articles published in English;
- studies assessing the diagnostic or prognostic value of CACS in patients with suspected or known CAD;
- use of CTA or non-contrast CT for CACS evaluation;
- reporting of relevant outcomes such as diagnostic accuracy (sensitivity/specificity) or prognostic endpoints (major adverse cardiac events, all-cause mortality).

Exclusion criteria included:
- non-human studies (n = 5);
- editorials, reviews without meta-analytic data, case reports, and conference abstracts (n = 18);
- studies lacking quantifiable outcomes or with insufficient methodological transparency (n = 7).

Data extraction and synthesis

The two independent reviewers gathered lead data such as study design, population characteristics, imaging methods, CACS thresholds, and the outcome measures. Any discrepancy among them was resolved either by consensus or adjudication from a third party. In meta-analytic pooling, a random-effects model was used for merging sensitivity, specificity, and hazard ratios (HRs) to accommodate heterogeneity.

Quality assessment

Methodological quality assessment of the included studies was performed by applying the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool for diagnostic studies and the Newcastle-Ottawa Scale (NOS) for prognostic ones. Both reviewers assessed bias risk, applicability, and validity of the study independently.

Results

Characteristics of included studies

A total of 14 studies were included in the qualitative analysis (Table 2), encompassing more than 81,743 participants across diverse geographic and demographic settings. The included populations comprised both symptomatic and asymptomatic individuals, patients with stable chest pain, diabetics, and those without a prior history of CAD. Most studies used non-contrast cardiac CT for CACS, while a subset incorporated both CACS and coronary CTA. Follow-up durations for prognostic assessment ranged from 2 to 10 years. The Agatston scoring system was consistently applied across studies, using standard categories: CAC = 0 (no calcification), CAC 1-99 (mild), CAC 100-399 (moderate), and CAC ≥ 400 (severe).

Diagnostic value

Among patients in low-to-intermediate risk categories, the addition of CACS significantly enhanced the diagnostic performance of CTA. The pooled sensitivity for detecting obstructive CAD (≥ 50% stenosis) was 88%

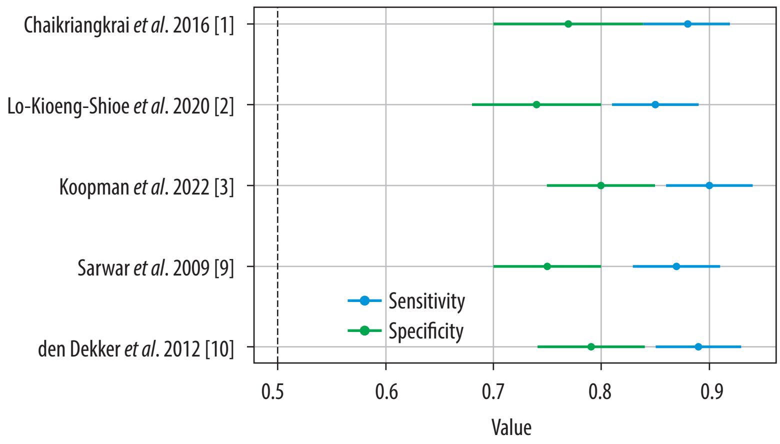

Figure 1. Forest plot of sensitivity and specificity of coronary artery calcium scoring and computed tomography angiography in the diagnosis of coronary artery disease

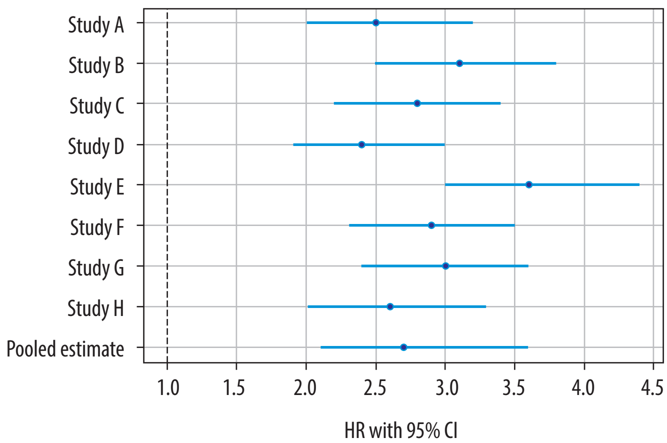

Figure 2. Forest plot of hazard ratios (HRs) for the prognostic value of coronary artery calcium score in predicting major adverse cardiac events

CI – confidence interval

(95% confidence interval [CI]: 84-91%) and pooled specificity was 77% (95% CI: 70-83%) when CACS was combined with CTA (Figure 1) [9,10]. The presence of any coronary calcification (CAC > 0) showed a strong association with obstructive CAD. However, the diagnostic accuracy of CTA was reduced in patients with very high calcium scores (CAC ≥ 400) due to blooming artifacts, which may obscure luminal visualization.

Prognostic value

Elevated CAC scores were consistently associated with increased risk of MACE. Patients with CAC ≥ 100 demonstrated a pooled HR of 2.7 (95% CI: 2.1-3.6) for future cardiac events compared with individuals with CAC = 0 (Figure 2) [11]. Conversely, a CAC score of zero was strongly associated with an excellent prognosis, with event rates remaining below 1% over a 5-year follow-up period [9,12].

Subgroup analyses

In asymptomatic individuals, a CACS of zero demonstrated a high negative predictive value for cardiac events [7]. However, even mild calcification (CAC 1-99) was associated with an increased risk of cardiac events in diabetic patients compared to non-diabetic individuals with similar scores [8,13]. The prognostic utility of CACS remained consistent across different age groups, sexes, and ethnic populations, although higher scores were more frequently observed in older individuals and males [10].

Discussion

This systematic review and meta-analysis further confirms that CACS provides significant diagnostic and prognostic value in the assessment of CAD. The findings consistently demonstrate that CACS, particularly when combined with coronary CTA, enhances early diagnosis and risk stratification across diverse populations, including asymptomatic individuals, diabetics, and patients with stable chest pain.

One of the most important findings of this study is that higher CAC scores are strong predictors of MACE. Patients with a CAC score ≥ 100 exhibited nearly a threefold increased risk of future cardiac events compared to those with a CAC score of zero [11]. These findings reinforce the role of CACS as a robust long-term prognostic marker and highlight its importance in guiding preventive strategies.

Equally significant is the prognostic implication of a CAC score of zero. The absence of coronary calcification is consistently associated with excellent clinical outcomes and very low event rates over intermediate follow-up periods [9,12]. This supports the concept of the "power of zero," which has important clinical implications in safely deferring further diagnostic testing or aggressive therapeutic interventions in low- to intermediate-risk patients.

Despite its advantages, certain limitations of CACS must be considered. In patients with extensive calcification (CAC score ≥ 400), the diagnostic performance of CTA may be compromised due to blooming artifacts, which can obscure luminal visualization and reduce specificity, potentially leading to false-positive findings [10]. However, while high calcium scores indicate elevated risk, they may simultaneously limit accurate anatomical assessment.

The combined use of CACS and CTA provides complementary information, improving overall clinical decision-making. While CACS reflects total plaque burden, CTA allows detailed evaluation of plaque composition and luminal stenosis. Discrepancies between the two modalities have been reported, such as high CAC scores with low Coronary Artery Disease – Reporting and Data System (CAD-RADS) scores due to masking effects of calcification, or low/zero CAC scores with high CAD-RADS scores in cases of non-calcified plaques. These observations highlight the importance of integrating both modalities for comprehensive cardiovascular assessment (Figure 3).

CACS also demonstrates consistent applicability across specific subgroups. In diabetic patients, even low levels of coronary calcification are associated with a significantly higher risk of cardiac events compared to non-diabetic individuals [8,13]. Furthermore, although calcium score distributions vary with age, sex, and ethnicity, its predictive value remains robust across different populations [10].

Despite the strengths of this meta-analysis, including a large pooled sample size and comprehensive evaluation of both diagnostic and prognostic outcomes, certain limitations should be acknowledged. Heterogeneity in study design, population characteristics, follow-up duration, and outcome definitions may introduce variability in the results. Additionally, not all included studies fully adjusted for conventional cardiovascular risk factors, which may act as confounders.

In conclusion, CACS is a reliable, non-invasive tool for both diagnosis and prognosis of CAD. Its integration with CTA enhances risk stratification and supports more precise, patient-specific clinical decision-making, reinforcing its role in contemporary cardiovascular imaging.

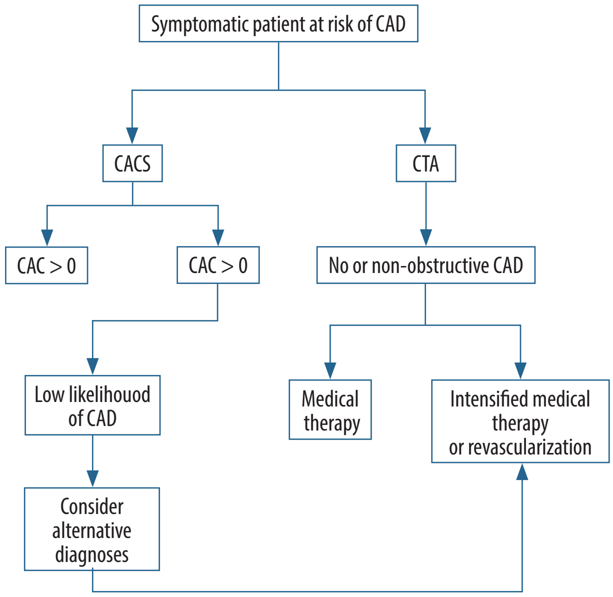

Figure 3. Integration of coronary artery calcium scoring (CACS) and coronary computed tomography angiography (CTA) in clinical decision-making for coronary artery disease (CAD)

CAC – coronary artery calcium

Conclusions

Our systematic review and meta-analysis highlights the significance of coronary calcium scoring as a non-invasive, cost-effective, and clinically useful tool for diagnosis and prognosis of CAD. CACS has been observed to be a highly predictive marker of MACE in a broad range of populations, particularly when its values exceed 100. CACS can also be used together with CTA to enhance the diagnostic accuracy of obstructive versus non-obstructive CAD, especially in low- to intermediate-risk patients.

One clinically significant finding is that a CAC score of zero is a reliable predictor of a very low risk of cardiovascular events in the short to intermediate term. This finding is increasingly being accepted to support the use of CACS as a gatekeeper to avoid exposing asymptomatic or low-risk persons to unnecessary invasive testing. Conversely, high CAC scores not only predict negative results but may demonstrate the potential failings of CTA interpretation because of blooming artifacts.

There is also evidence supporting the use of CACS in some high-risk subgroups including diabetics where even low calcium scores put the patient in a higher risk category. These insights may be used in clinical practice to personalize the risk stratification, guide therapeutic decision making, and streamline imaging resources.

In conclusion, CACS represents a central component of contemporary cardiovascular imaging protocols. The next phase of investigations should focus on establishing standard cutoff values, population-based risk profiles, and long-term outcome validation to further support the implementation of CACS in global CAD management.

Disclosures

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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