



ASSESSMENT OF CORONARY ARTERY DISEASE: EVALUATING THE RELATIONSHIP BETWEEN CORONARY CALCIUM SCORE AND STENOSIS PERCENTAGE USING CCTA

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ARTICLE INFO	ABSTRACT
<p>Keywords: CAD (coronary artery disease), Computed Tomography, Coronary Angiography (CTCA), and Coronary artery Calcium (CAC)</p> <p>Corresponding Author: Alishbah Roobi, Department of Physiology, The University of Faisalabad, Pakistan Email: asst.prof.physiology@tuf.edu.pk</p>	<p>Cardiovascular diseases are a major global issue, demanding accurate and timely diagnosis for effective intervention. Integrating advanced imaging techniques, such as computed tomography, coronary angiography (CTCA), and coronary artery calcium (CAC) Scores, has notably improved diagnostic precision and risk assessment. This research was conducted to find the association between coronary calcium score and stenosis percentage in coronary arteries, which is diagnosed by CT angiography in patients over 40 years old and with moderate symptoms of coronary artery disease. Data was collected from the Radiology Department of the Rawalpindi Institute of Cardiology, Rawalpindi. Eligible patients who met the inclusion criteria were identified, and relevant data was collected. The prevalence</p>

	of coronary artery disease (CAD) was highest in the 61-70 age group (33%). Male participants exhibited a higher CAD prevalence (55%) than females (45%). Hypertension was present in 66% of patients, 42% had a history of CAD in the family, Smoking was seen in 33%, and diabetes in 31%. The p-value representing the association between coronary calcium score categories and the Stenosis percentage diagnosed by CTCA is 0.01. This study concluded a significant positive correlation between coronary calcium score and Stenosis percentage in coronary arteries diagnosed by CT angiography.
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Introduction

Coronary artery disease, also known as CAD, still stands as the dominant reason for morbidity and mortality across continents (1). Although much has been discussed about the relationship between coronary calcium score (CCS) and stenosis in coronary artery disease (CAD), this study aims to provide a new perspective: the relationship between CCS and the degree of stenosis diagnosed through coronary computed tomographic angiography (CCTA) (2). It opens up possibilities for narrowing further the CAD risk-stratification and diagnostic workup with the new imaging and artificial intelligence (AI) tools. Furthermore, this study aims to ultimately determine how CCS can enhance CCTA's accuracy in detecting CAD, with the potential to employ various treatment and clinical management strategies (3,4). Given that most research has been concentrated on individual techniques, this study is the first to focus on the synergistic effects between CCS and CCTA (5). The combination of using these two complementary diagnostics will enhance the understanding of how the two modalities work synergistically in assessing coronary stenosis and may ultimately lead to more personalized patient management strategies through more effective management (6). Coronary Artery Disease (CAD) is primarily an outcome of plaque buildup in the coronary arteries, causing narrowing and hardening of the arteries, which restricts blood flow to the heart (7). These plaques are primarily composed of a mixture of fatty substances, cholesterol, cellular waste products, calcium, and fibrin, which facilitate the atherosclerotic process underlying CAD (8). The obstruction of the artery by the accumulation of these plaques inhibits the delivery of oxygen to the myocardium and may lead to myocardial infarction (heart attack) (9).

For many years, catheter coronary angiography (CCA) has been the conventional diagnostic tool of obstructive CAD with excellent sensitivity and specificity, but with a very remote chance of complications (10). Noninvasive imaging methods, such as computed tomography coronary angiography (CTCA), have gained popularity due to their high diagnostic yield, providing detailed 3D images of the coronary vessels (11). CCTA enables the accurate measurement of coronary stenosis and provides additional information regarding plaque composition, including the degree of calcification (12). However, while CCTA works very well, it may not fully reflect the atheroma burden in those cases with non-calcified plaques (13). Coronary calcium scoring is an imaging technique that quantifies the amount of calcium within coronary arteries, facilitating an evaluation of the presence and severity of coronary atherosclerosis (14). In prior studies, CCS has been validated as a predictor of cardiovascular risk, especially in patients at intermediate risk (15). The calcium score is simply a numerical indicator that reflects the atherosclerotic burden and helps classify patients at cardiovascular risk (16). Nonetheless, one must recognize that CCS identifies only calcified plaques, and CCS can't detect their soft or non-calcified counterparts, which may also represent disease progression for coronary arteries (17). In our study, we aim to better understand how the CCS can complement CCTA, particularly in situations where calcified plaques alone may not accurately represent the overall disease burden. We strive to gain a deeper understanding of how CCS relates to stenosis observed on CCTA, thereby elucidating how the two modalities can provide a more comprehensive assessment of CAD and ultimately improve the accuracy of diagnosis and precision of treatment decisions.

Methodology

Study Design and Participants: This cross-sectional study was conducted in the Radiology Department of the Rawalpindi Institute of Cardiology (RIC) in Rawalpindi, Pakistan, from July 15, 2023, to January 15, 2024. A total of 104 subjects aged 40 years or older with mild to moderate symptoms of coronary artery disease (CAD) were then selected, and all were subjected to both Coronary Computed Tomography Angiography (CCTA) and coronary calcium scoring (CCS) to assess the relationship between coronary calcium scores and the degree of stenosis.

Inclusion criteria: Participants above 40 years with mild to moderate symptoms of CAD were suitable for CCTA and CCS.

Exclusion criteria: Participants were excluded if they had previous CABG surgery or if they had severe coronary events or any other condition that could interfere with the diagnosis.

Ethical approval for this study was obtained from the Institutional Review Board (IRB) of Government College University, Faisalabad, and informed consent was obtained from all subjects. Data were anonymized and securely stored to maintain patient confidentiality and in line with relevant data protection legislation.

Coronary Calcium Scoring Procedure

Coronary calcium scores were generated using a multi-detector computed tomography (MDCT) scanner, specifically the Toshiba Aquilion 64-row detector-type scanner provided by Toshiba Medical Systems, Japan. Patients were placed in the supine position on a scanner table under attached ECG leads to monitor their heart rates during scoring procedures. No contrast media were administered during calcium scoring procedures.

The exposure is relatively low and is achieved through multiple-slice scanning, which takes place from the base to the apical part of the heart. Images are reconstructed in 3 mm-thick axial slices, which are intended to be transferred to the Vitrea 2 Workstation for calcium detection. The manual tagging of calcium located in the coronary arteries is performed on the reconstructed images using the Agatston scoring system, which assigns a numerical value to the amount of calcified plaque present in the coronary arteries. This procedure accurately measures the burden of atherosclerosis in the coronary arteries and is used for risk stratification of cardiovascular events (18).

Coronary Computed Tomography Angiography (CCTA)

All study participants, both selected and non-selected, were given instructions to fast for at least four hours before the actual CCTA to minimize the adverse effects of the contrast medium. The standard protocol for using NTG for coronary artery dilation, combined with beta-blockers to slow the heart rate and facilitate the procedure, was followed. For this scan, patients were placed in a supine position with their arms elevated above their heads. A cannula was inserted into the antecubital fossa above the cubit, using a 20G cannula for intravenous (IV) administration. A total of 80 mL of a non-ionic contrast (350 mg iodine/mL) was injected at a rate of 4 mL/sec, followed by a 40 mL saline flush. The scanning protocol included data acquisition at 30%, 50%, and 70% of the RR interval, as established in a cardiac cycle, to minimize the effects of motion artifacts. The captured images were processed using a Vitrea 2 Workstation, which enables the generation of detailed three-dimensional images for assessing coronary artery stenosis. Two

independent, qualified radiologists double-checked the degree of stenosis to minimize potential bias in this critical measurement.

Statistical Analysis

The data from participants, including demographic information, medical history, coronary calcium scores, and stenosis percentages, were analyzed via Stata 13 and Epi Info 7. Descriptives were applied to summarize demographic data, with categorical variables (e.g., CCS categories and stenosis percentage) assessed using the Chi-square test. To enhance statistical rigor, we also incorporated multiple regression analyses to adjust for potential confounders, including age, sex, hypertension, smoking, and diabetes, in the relationship between calcium score and stenosis percentage, thereby yielding a more robust statistical analysis. Such an action was intended to provide a more precise definition of CCS's predictive power in diagnosing CAD and assessing the grade of stenosis, as well as evaluating other indices of effect size, such as odds ratios and/or correlation coefficients, which quantify the strength of association between CCS and the percentage of stenosis. This additional analysis was undertaken to help elucidate, possibly, the size and direction of the relationship between these two diagnostic entities, as was elucidated.

Results

Age Group of Patients

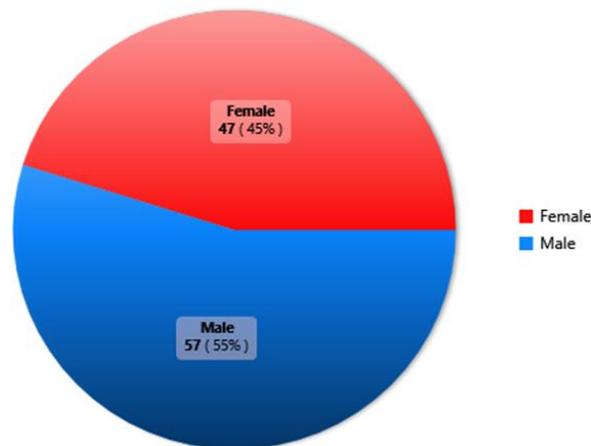
The frequency and percentage of patients in various age groups were calculated. Among the 104 patients, 22% belonged to the 41-50 age group, 28.8% to the 51-60 age group, 33.3% to the 61-70 age group, and 15.3% to the 71-80 age group. The patient distribution by age group is presented in Table 1.

Table 1: Shows the age group of patients

Age Group	Frequency	Percent	Exact 95% LCL	Exact 95% UCL
41-50	23	22.12%	14.57%	31.31%
51-60	30	28.85%	20.38%	38.55%
61-70	35	33.65%	24.68%	43.58%
71-80	16	15.38%	9.06%	23.78%
Total	104	100.00%		

Gender of Patients

The percentage and number of patients belonging to different gender groups were computed. The patient category consisted of 55% males and 45% females. The percentage of patients, categorized by gender, is illustrated in Figure 1, which shows the distribution of male and female patients.



Frequency of causes

Patients were calculated to have percentages and numbers for patients having hypertension, a family history of CAD, smoking, and diabetes. Interestingly, only 42% of the participants had a family history of CAD, while 66% had hypertension. Smoking was seen in 33% of the participants, while 67% were non-smokers. Diabetes mellitus was seen among 31% of the patients. The causes of CAD are described in Figure 2, which shows the distribution of causes for coronary artery disease among the participants.

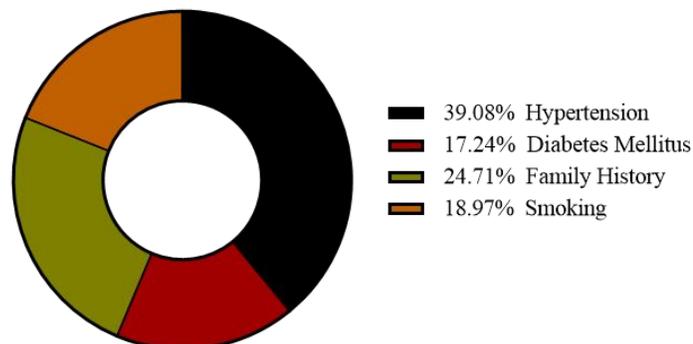


Figure 2: Frequency of causes of CAD

Clinical findings

Coronary Artery Calcium Score

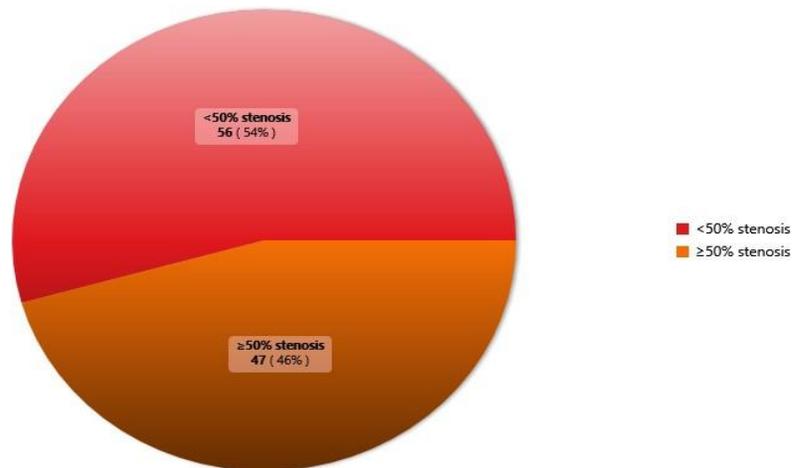
Approximately 40% of the patients had a calcium score of zero; 11% fell within the 1-100 calcium score category; 29% had a calcium score of 101-300; and approximately 22% had a calcium score greater than 300. The distribution of calcium scores among study participants is illustrated in Table 2.

Table 2: Categories of Coronary Calcium Score of Patients

Coronary Calcium Score	Frequency	Percent	Exact LCL	95% Exact UCL
Zero	40	38.5%	29.1%	48.5%
1-100	11	10.6%	5.4%	18.1%
101-300	30	28.8%	20.4%	38.6%
More than 300	23	22.1%	14.6%	31.3%
TOTAL	104	100.0%		

Stenosis percentage

The number and percentage of patients falling into the two categories of stenosis percentage are shown in Figure 3. Fifty-four percent of patients had stenosis of less than 50%, while 46% had stenosis of 50% or greater.



Association of Coronary Calcium Score and Stenosis Percentage

The two principal variables of this study, CAC score and stenosis percentage association, are shown in this table. The variables are categorical, and a p-value of 0.01 was calculated using the Chi-squared formula (Table 3).

Table 3: Association of Stenosis and Coronary Calcium Score

Coronary Calcium Score	<50% Stenosis	≥50% Stenosis	TOTAL
Zero	34	6	40
1-100	8	3	11
101-300	12	17	29
More than 300	2	21	23
TOTAL	56	47	103
Chi-square	37.933		
Probability (p-value)	0.010		

Discussion

Advancements in artificial intelligence (AI) are transforming the field of cardiovascular Medicine, particularly in the context of coronary artery disease (CAD). Machine learning AI algorithms are gradually being integrated into diagnostic workflows, promising an enhancement of CAD risk assessment accuracy. "Artificial Algorithms Outperform Traditional Models in Predicting Coronary Artery Disease," according to Arquivos Brasileiros de Cardiologia, states that AI analyzes parameters such as Coronary Artery Calcium (CAC) scores and outperforms classical models in predicting CAD (19). AI models can recognize subtle patterns in imaging data that are often missed by human experts, leading to more nuanced interpretations of coronary health. The integration of artificial intelligence and coronary calcium scoring offers a significant opportunity for improvement in risk stratification. Although CCS is regarded as a reliable, non-invasive method for measuring the presence of coronary atherosclerosis, combining CCS with AI algorithms will further enhance diagnostic productivity. AI can handle large datasets from various imaging modalities, facilitate the interpretation of CAC scores, and improve the advancement of disease forecasting by identifying important clinical variables that capture more than just traditional measurements. These AI-enhanced tools will provide not only more precise

but also more cost-effective risk evaluation for early diagnosis and personalized treatment plans. Yet, beyond these, study by D. T. Reddy and its colleagues show that, apart from assisting HS in establishing the AI-based diagnostic potential of CAC, the flow prospect present in this context defines the eventual improvement of early CAD and disease course prognosis (20). Integrating AI may enable clinicians to access CAC data even faster and more accurately, thereby improving patient outcomes through timely intervention. Good innovation is a darling of growing avenues for CAD diagnostics. This research offers valuable insights into the relationship between coronary calcium scores (CAC) and percentage stenosis in the diagnosis of coronary artery disease (CAD). Unlike most traditional diagnostic investigations that focus on a single criterion, this approach combines information from both CCTA and CCS (21). The present findings provide a strong correlation with increasing CAC scores and progression of coronary stenosis, most notably starting at scores of more than 300, with nearly all cases having some significant stenosis. This study provides new value by defining the relationship, not merely the previously established one, between CAC and stenosis, but also by exploring the new role of non-calcified plaques that would otherwise not be accessible to CAC on its own. Additionally, this study examines variations between CAC score categories in terms of how CCS predicts the severity of CAD and identifies patients at risk for severe stenosis. This will provide particular insight into patients who fall into intermediate-risk categories, as the CAC score may offer additional information for clinical decision-making (22). These results related to K. M. Abdelrahman and its colleagues work that CCS will be a further component of the conventional approach for CAD diagnosis and risk assessment, complementing those provided by methods such as CCTA (23). Thus, for the first time, this research will examine CCS and CCTA together with CAD diagnostic potential. In that sense, it will take a more integrated approach to CAD, rather than unifying these two competing techniques, to achieve improved clinical outcomes. In addition, the findings of this study suggest that AI-based analysis of such diagnostic tools is likely to represent a significant advancement in CAD prediction and management. Establishing CAD with non-invasive techniques adopted to date, Coronary Computed Tomography Angiography (CCTA) and Coronary Calcium Scoring (CCS) offer specific utilities. While both are known methods for diagnosing CAD, a significant difference between CCTA and CCS is that CCTA provides much more detailed and reliable imaging of the coronary arteries, identifying both calcified and non-calcified plaques. In contrast, H. Liu, A. Wingert study indicate that CCS quantifies only the

amount of calcified plaque, which is highly relevant to the degree of atherosclerosis (24). This study aimed to compare the efficiency of CCTA versus CCS in assessing the severity of CAD based on the relationship between CAC scores and stenosis percentage. Our results show that both CCTA and CCS complement each other well in the evaluation of CAD. In CCTA assessment, extensive visualization of the coronary vessels is observed. In contrast, the CCS is a simple, non-invasive measure for the existence and extent of coronary calcification, which correlates strongly with stenosis. It was noted that patients with a CAC score of 0 had stenosis levels of <50% in general, but that those patients with a CAC score >300 generally had significant stenosis ($\geq 50\%$). This finding further strengthens the already established diagnostic capacity of CAC scores to identify at-risk patients and predict CAD severity, making CCS an excellent risk stratification tool, particularly when combined with CCTA. CCS could also eliminate the need to send patients with low or zero calcium scores to unnecessary follow-up tests such as CCTA, which in turn could lower healthcare costs without compromising the quality of diagnostics. To conclude, it can be said that both CCTA and CCS are significant modalities in the diagnosis of CAD, as CCTA provides comprehensive images while CCS offers a less expensive, non-invasive assessment of atherosclerotic burden. The integration of the two modalities, particularly with the addition of AI, will lead to more accurate diagnoses and informed clinical decisions.

Limitations

This study has several limitations that warrant acknowledgment. First, we did not specifically address the sensitivity, specificity, or positive or negative predictive values of Coronary Calcium Scoring (CCS). These parameters are essential for assessing any screening tool, including the CCS, and their omission is a definite limitation to this study. If these values had been more comprehensively evaluated, then a clearer picture of the CCS's diagnostic performance for coronary artery disease (CAD) would have ensued. CCS is compared as a screening method with Coronary Computed Tomography Angiography (CCTA) instead of the gold standard method of Catheter-based Coronary Angiography (CCA). CCA is recognized as the reference standard for diagnosing obstructive CAD, and when it was excluded from our comparative analysis, we limited our ability to assess the performance of CCS in comparison to this accepted method. Future studies should compare cases between CCA and CCS to determine the diagnostic value with some accuracy and assess its clinical value.

Conclusion

This study established a significant correlation between the Coronary Calcium Score (CCS) and percent stenosis in patients with coronary artery disease (CAD). Our findings indicated that higher CAC scores were associated with higher stenosis severity, especially in patients having CAC scores higher than 300, with a general presence of stenosis $\geq 50\%$. On the contrary, in patients with a score of 0 or low scores, stenosis was likely to be $< 50\%$, further emphasizing the potential of CCS in non-invasively and cost-effectively estimating CAD severity and the need for further diagnostic tests. This study has implications for the clinician. Coronary Calcium Scoring (CCS), combined with Coronary Computed Tomography Angiography (CCTA), helps refine risk assessment and treatment strategies for coronary artery disease (CAD). By predicting stenosis, CCS allows clinicians to classify patients at high risk for severe types of CAD, thereby enabling early intervention and more targeted therapies. Notably, CCS could reduce the number of CCTAs performed on patients who are at low risk, thereby minimizing healthcare costs and improving patient management. Further research should aim to integrate AI and machine-learning techniques with CCS and CCTA to enhance CAD diagnosis and risk prediction. AI could be developed for the analysis of large datasets, the identification of hidden patterns, and the improvement of predictive accuracy of CCS for CAD severity. Multivariate regression and other statistical models can be applied to adjust for potential confounders and refine the predictive models of disease progression. By incorporating AI into commonplace clinical practice, personalized, efficient, and accurate CAD management can be realized, thereby improving patient outcomes and alleviating some burden from the healthcare system.

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Ethical Declaration

All methods conducted in this study were by the ethical standards stated by the IRB for human subject research. No animal experiments were performed. All participants gave informed consent, and this study was approved by the IRB of the Government College University, Faisalabad.

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