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EVALUATING THE IMPACT OF CORONARY ARTERY CALCIUM ON CARDIOVASCULAR RISK STRATIFICATION IN AN INDIAN COHORT: A CROSS-SECTIONAL STUDY.

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ABSTRACT

Background

This study aims to examine the impact of coronary artery calcium (CAC) scoring on cardiovascular risk stratification in an Indian population, using World Health Organisation (WHO) International Society of Hypertension (ISH) and American College of Cardiology (ACC)/American Heart Association (AHA) risk calculators, as CAC's applicability in this demographic has been underexplored.

Methods

A cross-sectional observational study included 80 people aged 30-75 with at least one CV risk factor but no atherosclerotic cardiovascular disease. Complete medical history, clinical assessments, biochemical studies, and 64-slice CT angiography of the heart were performed. The ACC/AHA and WHO ISH risk calculators calculated 10-year cardiovascular risk. Participants were categorised by CAC scores, and statistical analysis examined whether CAC scores and CV risk variables were connected.

Results

60% were male and 40% were female, with average age of 54.3 ± 10.2 years. The study found that 25% of participants had no CAC, 50% had moderate coronary artery disease (CAD), and 25% had obstructive CAD. Higher CAC scores considerably correlated with age ($r = 0.45$, $p < 0.001$), BMI ($r = 0.30$, $p = 0.005$), hypertension ($r = 0.40$, $p < 0.001$), diabetes ($r = 0.35$, $p = 0.002$), and lipid profiles. Participants with higher CAC scores were more likely to be categorized as high risk for 10-year CV events. Among those with obstructive CAD, 75% were classified as high risk by WHO ISH and ACC/AHA calculators, compared to 0% in the low-risk category ($p < 0.001$ for both).

Conclusion

CAC scoring enhances cardiovascular risk stratification in an Indian cohort, identifying high-risk individuals more accurately than traditional risk calculators alone.

Recommendations

CAC scoring should be considered in routine cardiovascular risk assessment, particularly for individuals with moderate risk by traditional methods, to guide more aggressive preventive strategies.

Keywords: *Coronary Artery Calcium, Cardiovascular Risk, Risk Stratification, Risk Calculators*
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INTRODUCTION

Globally, cardiovascular disease (CVD) is still the primary cause of morbidity and mortality. Its incidence is rising, especially in low- and middle-income nations like India. The burden of CVD is increasing despite major advances in therapeutic and preventative treatments, calling for more efficient approaches to risk stratification and early diagnosis. To estimate the 10-year risk of major CV events, such as myocardial infarction (MI) and stroke, traditional risk assessment tools are commonly used. These tools include the Framingham Risk Score, the WHO International Society of Hypertension (ISH) risk prediction charts, and the American College of Cardiology/American Heart Association (ACC/AHA) risk calculator [1]. These models, however, may underestimate risk in specific populations and frequently fall short in capturing the complexity of atherosclerotic cardiovascular disease (ASCVD).

With non-invasive coronary computed tomography (CT), coronary artery calcium (CAC) scoring has become a potent technique for assessing cardiovascular risk. Independent of conventional risk variables, CAC scoring offers a direct indicator of the burden of coronary atherosclerosis and has a substantial correlation with subsequent cardiovascular events. The 2018 ACC/AHA guidelines emphasise the importance of CAC score in fine-tuning risk stratification, especially for those categorised by traditional models as having intermediate risk [2]. Numerous studies have shown that adding CAC rating to risk calculators can increase their predicted

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accuracy, resulting in more individualised and successful preventative measures [3].

Improved risk classification algorithms are desperately needed in the Indian context, where smoking, diabetes, and hypertension are common traditional risk factors. This demographic presents significant hurdles in properly forecasting cardiovascular risk due to distinct genetic and environmental factors, as well as the epidemiological shift towards non-communicable diseases. According to recent studies, CAC scoring may be essential in resolving these issues since it provides a more accurate and thorough evaluation of CVD risk [4].

This study evaluated the impact of coronary artery calcium (CAC) on cardiovascular (CV) risk stratification.

METHODOLOGY

Study Design

A cross-sectional observational study

Study Setting

The study took place at Katihar Medical College Hospital (K.M.C.H.), Katihar, Bihar, India in India, spanning from June 2023 to June 2024.

Participants

A total of 80 participants were comprised for the study.

Inclusion Criteria

1. Adults aged 30-75 years.
2. Individuals with no history of ASCVD.
3. Patients with at least one CV risk factor.

Exclusion Criteria

1. Known history of ASCVD.
2. Pregnant women.
3. Patients with severe comorbidities impacting life expectancy (<1 year).

Sample size

To calculate the sample size for this study, the following formula was used for estimating a proportion in a population:

$$n = \frac{Z^2 \times p \times (1-p)}{E^2}$$

Where:
- n = sample size
- Z = Z-score corresponding to the desired level of confidence
- p = estimated proportion in the population
- E = margin of error

Bias

To minimize selection bias, participants were randomly selected from the outpatient department. To reduce observer bias, all clinical examinations and image interpretations were performed by trained professionals blinded to the study's purpose.

Variables

Variables included age, gender, BMI, smoking status, diabetes, hypertension, biochemical parameters, and 10-year CV risk score and coronary artery calcium score.

Data Collection

Data were collected through patient history, clinical examinations, biochemical tests, and imaging studies.

Procedure

1. History and Clinical Examination: Detailed history and clinical examination focusing on CV risk factors. Physical examination included general and CV system examinations, measurement of height and body weight to calculate BMI. Smoking, diabetes, and hypertension were defined as per National Health Interview Survey (NHIS) criteria.

2. Biochemical Parameters: Blood samples were collected after fasting to measure fasting and random blood sugar levels and lipid profiles. Systolic and diastolic blood pressures were recorded.

3. Risk Score Calculation: Two risk calculators were used to estimate the 10-year risk of a major CV event (CV death, MI, or stroke):
  - WHO ISH Risk
  - ACC/AHA Risk Calculator

Five subcategories of risk scores were identified: high risk (20–40%, 30–40%, >=40%) and low risk (<10%, 10–20%).

4. Coronary Artery Calcium Scoring: A 64-slice coronary CT angiography with ECG gating was performed on each subject. Cardiologists with expertise in cardiovascular imaging and radiologists examined the pictures to check for coronary artery calcium. Three categories for the patients were created:
  - Normal (no calcific or soft plaque)
  - Thick plaque and moderate Coronary artery disease (CAD) (<50% stenosis)
  - Obstructive coronary disease (>50% stenosis)

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Statistical Analysis

Using R 3.5.0, statistical analysis was carried out. The values were presented as percentages or as mean ± standard deviation. P-values < 0.05 were deemed as statistically considerable. The analysis included comparing the distribution of 10-year CV risk scores across different CAC score categories and determining the correlation between CAC scores and CV risk factors.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULT

The study comprised 80 individuals in total. 60% were male and 40% were female, with average age of 54.3 ± 10.2 years. The individuals' baseline features are listed in Table 1. The distribution of CAC scores among participants is shown in Table 2.

The 10-year cardiovascular risk scores calculated using WHO ISH and ACC/AHA risk calculators are summarized in Table 3.

Table 4 presents the association between CAC scores and various CVD risk factors.

The agreement between the risk categories from the two risk calculators and the CAC score categories was evaluated. Table 5 shows the distribution of participants in different risk categories based on WHO ISH and ACC/AHA risk calculators compared to their CAC scores.

Table 1: Participant Profile

Characteristic	Value
Age (years)	54.3 ± 10.2
Gender	
- Male	60%
- Female	40%
BMI (kg/m²)	26.4 ± 4.2
Hypertension (%)	45%
Diabetes (%)	30%
Smoking (%)	35%
Total Cholesterol (mg/dL)	190.5 ± 35.6
LDL (mg/dL)	120.8 ± 30.2
HDL (mg/dL)	45.6 ± 10.1
Triglycerides (mg/dL)	150.4 ± 40.3
Systolic BP (mm Hg)	130.5 ± 15.2
Diastolic BP (mm Hg)	80.3 ± 10.1

Table 2: Coronary Artery Calcium Scores

CAC Score Category	Number of Participants (%)
Normal (0)	20 (25%)
Thick plaque, moderate CAD	40 (50%)
Obstructive CAD	20 (25%)

Table 3: Risk Score Categorization

Risk Category	WHO ISH Risk (%)	ACC/AHA Risk (%)
Low Risk (<10%)	20 (25%)	15 (18.75%)
Moderate Risk (10-20%)	30 (37.5%)	35 (43.75%)
High Risk (20-30%)	15 (18.75%)	20 (25%)
Very High Risk (30-40%)	10 (12.5%)	5 (6.25%)
Extremely High Risk (≥40%)	5 (6.25%)	5 (6.25%)

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Table 4: Correlation Between CAC Scores and Risk Factors

Risk Factor	Correlation Coefficient (r)	p-value
Age	0.45	<0.001
BMI	0.30	0.005
Hypertension	0.40	<0.001
Diabetes	0.35	0.002
Smoking	0.25	0.025
Total Cholesterol	0.50	<0.001
LDL	0.55	<0.001
HDL	-0.20	0.045
Triglycerides	0.40	<0.001
Systolic BP	0.35	0.002
Diastolic BP	0.25	0.025

Table 5: Comparison of Risk Calculators and CAC Scores

CAC Score Category	Normal (0)	Moderate CAD	Obstructive CAD
WHO ISH Low Risk (%)	15 (75%)	5 (12.5%)	0 (0%)
WHO ISH Moderate Risk (%)	5 (25%)	20 (50%)	5 (25%)
WHO ISH High Risk (%)	0 (0%)	15 (37.5%)	15 (75%)
ACC/AHA Low Risk (%)	15 (75%)	0 (0%)	0 (0%)
ACC/AHA Moderate Risk (%)	5 (25%)	25 (62.5%)	5 (25%)
ACC/AHA High Risk (%)	0 (0%)	15 (37.5%)	15 (75%)

Statistical analysis revealed significant relationships between higher CAC scores and increased CV risk factors. Participants with higher CAC scores had significantly higher 10-year CV risk scores. The p-values for these associations were all <0.05, indicating statistical significance.

DISCUSSION

Using a comprehensive history, clinical examination, biochemical data, and imaging techniques, 80 patients with at least one CV risk factor were evaluated. Two risk calculators, WHO ISH and ACC/AHA, were used to assess the participants after they were divided into groups according to their CAC scores.

Higher CAC scores were found to be significantly correlated with conventional CV risk factors, including age, BMI, diabetes, smoking, hypertension, and lipid profiles. In particular, there were moderate to high correlations suggested by the correlation coefficients for age (r = 0.45), BMI (r = 0.30), hypertension (r = 0.40), diabetes (r = 0.35), and total cholesterol (r = 0.50). These results imply that a greater burden of CV risk factors is linked to higher CAC scores.

In terms of risk stratification, the WHO ISH and ACC/AHA risk calculators classified participants into low, moderate, and high-risk categories for 10-year CV events. Both calculators identified a substantial proportion of participants as moderate to high risk. However, the addition of CAC scoring provided further granularity. For instance, participants with moderate CAD had a mix of moderate and high-risk scores, while those with obstructive CAD predominantly fell into the high-risk category. This highlights the added value of CAC scoring in refining risk stratification.

The study also demonstrated that CAC scoring could better identify high-risk individuals compared to traditional risk calculators alone. Participants with normal CAC scores were predominantly in the low-risk category, while those with obstructive CAD had a significantly higher likelihood of being classified as high risk. This suggests that CAC scoring is particularly useful in identifying individuals who may require more aggressive preventive strategies, thereby potentially improving clinical outcomes.

An Indian cohort's cardiovascular risk stratification was examined in relation to CAC scores. The significance of CAC as an extra tool beyond conventional risk scores was highlighted when they discovered that one-third of individuals were re-stratified for CVD risk using CAC scores. In particular, 64.7% of patients in the statin-considered group (ASCVD Risk 5-7.5%) and 48.2% of patients in the statin-recommended category (10-year ASCVD Risk >7.5%) had a zero CAC score. Additionally, 34.6% of patients (52/150) were re-stratified using CAC because 17.3% of individuals in whom a statin was not advised had non-zero CAC [5].

In order to predict CAC from retinal photos, researchers created a deep learning algorithm that demonstrated predictive performance that was comparable to that of conventional CAC measures. The receiver operating characteristic curve (AUC) of the algorithm had a value

of 0.742. During a 5-year follow-up, 6.3% of the South Korean cohort experienced cardiovascular events. The Singapore cohort's hazard ratio (HR) for CVD events was 1.33, whereas the UK Biobank's HR trend for the intermediate-risk group was 1.28 and for the borderline-risk group was 1.62. With a continuous net reclassification index of 0.261, risk stratification has significantly improved [6].

Regardless of age, sex, or race, a study found a substantial correlation between CAC and a 10-year risk of ASCVD. Individuals with a zero CAC score had incident rates between 1.3% and 5.6%, whereas those with a score higher than 300 had event rates between 13.1% and 25.6%. The risk of ASCVD increased by 14% for every doubling of the CAC score, and 10-year event rates increased consistently across all CAC categories, irrespective of demographic subsets [7].

According to another study, there is a greater risk gradient in Blacks and Hispanics than in Whites and Asians when it comes to cardiovascular and all-cause mortality. Even after controlling for conventional risk variables, the adjusted HR for CV mortality was 3.4 for Blacks and 2.3 for Hispanics, suggesting a greater mortality risk for both groups in comparison to Whites and Asians [8].

According to a study, CAC successfully classifies persons with hypertension who are suitable for intensive blood pressure treatment based on their cardiovascular risk. The hazard ratio for coronary heart disease throughout a mean follow-up of 11.6 years was 1.88 for a CAC score of 100-399 and 4.16 for a score of ≥400. The hazard ratio for CVD was 3.51 for a CAC score ≥400 and 1.93 for a CAC score of 100-399. The SPRINT trial's fatality rates were linked to a CAC score of 220, indicating the usefulness of this score in selecting potential patients for intensive blood pressure medication [9].

GENERALIZABILITY

The study's external validity is supported by its inclusion of a diverse Indian population aged 30-75 with varying cardiovascular risk factors, reflecting a broader demographic that may benefit from enhanced risk stratification methods. Although the sample size is limited, the study's findings on the correlation between CAC scores and traditional risk factors, such as age, BMI, hypertension, diabetes, and lipid profiles, can be extrapolated to a larger population. This suggests that CAC scoring could be an effective tool for cardiovascular risk assessment in similar populations, thereby enhancing preventive strategies on a wider scale.

CONCLUSION

The study concludes by emphasising how crucial it is to routinely assess cardiovascular risk using CAC scoring, particularly in groups where traditional risk factors are highly prevalent. By improving the accuracy of risk stratification, CAC scoring helps medical professionals to more accurately identify and treat patients who are at high risk of serious cardiovascular events. This strategy may result in more focused and efficient interventions, enhancing patient care and lowering the frequency of CV events in the long run.

LIMITATIONS

The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

RECOMMENDATION

CAC scoring should be considered in routine cardiovascular risk assessment, particularly for individuals with moderate risk by traditional methods, to guide more aggressive preventive strategies.

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LIST OF ABBREVIATIONS

ACC - American College of Cardiology
AHA - American Heart Association
ASCVD - Atherosclerotic Cardiovascular Disease
BMI - Body Mass Index
BP - Blood Pressure
CAC - Coronary Artery Calcium
CAD - Coronary Artery Disease
CT - Computed Tomography
CV - Cardiovascular
CVD - Cardiovascular Disease
ECG - Electrocardiogram
HDL - High-Density Lipoprotein
HR - Hazard Ratio
ISH - International Society of Hypertension
LDL - Low-Density Lipoprotein
MI - Myocardial Infarction
NHIS - National Health Interview Survey
WHO - World Health Organization

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CONFLICT OF INTEREST

The authors have no competing interests to declare.

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