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Reclassification of Cardiovascular Risk Using Coronary Artery Calcium Scoring in a Preventive Cardiology Clinic Population

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Abstract

Introduction: South Asians have the highest rates of premature ASCVD globally, a phenomenon not entirely explained by traditional risk factors. Effective risk assessment is crucial for primary prevention, guiding treatment strategies. US prevention guidelines advocate for pooled cohort equations for risk estimation, promoting shared decision-making. Coronary Artery Calcium (CAC) score, a specific marker of plaque burden, independently predicts CHD, stroke, and ASCVD events, even in low-risk individuals. This study assesses how incorporating calcium scoring affects patient risk classification compared to ASCVD risk scoring alone.

Material and Methods: A total of 204 consecutive asymptomatic subjects, who underwent comprehensive screening in a primary prevention clinic were included. Standard risk factors participants were evaluated by specialized primary care providers, underwent a comprehensive assessment encompassing detailed history, physical examination, and laboratory evaluation. Routine Coronary Artery Calcium Scoring (CACS) was a standard part of this evaluation. 10-year risk ASCVD was calculated using baseline data according to the Pooled Cohort Equations, then categorized as low (<5%), intermediate (5 to 19.9%), and high risk (≥ 20%) group. CAC score was categorized as 0 and >0.

Result: Mean Age, BMI, total cholesterol, ASCVD score, Calcium score were, 52 ± 9, 28.9 ± 5.3, 178 ± 45, 10.4 ± 10.8 and 176 ± 490 respectively. In ASCVD risk assessment, 79 individuals were categorized as low-risk (<5%), 90 as intermediate risk (5–19.9%), and 35 as high risk (≥ 20%). Concurrently, based on their CAC score, 108 individuals had a normal score (0), while 96 had an abnormal score (>0). When CAC risk categorization were applied, notable shifts would occur in ASCVD risk categories. 42 subjects would move from the 2nd to the 1st category, and 29 from the 3rd to the 2nd. Additionally, 6 individuals (3%) would experience a 2-category downgrade, while 19 (9%) would undergo a 1-category upgrade. In total, 47% of subjects could see their ASCVD risk category change if CAC risk categorization were implemented.

Conclusion: In a primary prevention screening program of asymptomatic patients, addition of CACS results in significant risk reclassification emphasizing the importance of CACS for more accurate and impactful risk evaluation and prevention of CHD.

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Introduction

Cardiovascular Disease (CVD) remains a leading cause of morbidity and mortality worldwide, with Atherosclerotic Cardiovascular Disease (ASCVD) being the most common form. Traditional risk factors such as age, sex, smoking, hypertension, dyslipidemia, and diabetes have been extensively studied and incorporated into risk assessment algorithms. However, these factors are inadequate in identifying all individuals who are at risk of developing CVD, particularly in high-risk populations such as South Asians, who have higher rates of premature ASCVD among other ethnic groups in the world [1,2]. This highlights the need for additional tools to refine risk stratification and guide treatment decisions in this population.

Proper risk assessment plays a crucial role in primary prevention of ASCVD, with the pooled cohort equations recommended in current US prevention guidelines for blood pressure and cholesterol management [3].

Recent studies have suggested that Coronary Artery Calcium (CAC) scoring could serve as a promising tool for risk stratification in primary prevention of CVD [4,5]. Coronary artery calcium is measured semi automatically by non-contrast cardiac Computed Tomography (CT) [6] and typically quantified by the Agatston score, which factors in the density and area of the calcium. CAC is a useful surrogate measure of total coronary atherosclerotic burden and therefore "arterial age [7]." CAC scoring is a highly specific marker of atherosclerotic plaque burden in the coronary arteries and has been found to be a robust predictor of future Coronary Heart Disease (CHD), stroke, and ASCVD events, independent of traditional risk factors [8,9]. The use of CAC scoring has been shown to reclassify patients' risk of CVD and aid in treatment decision-making, particularly in those who fall into the borderline or intermediate risk categories based on traditional risk factors [10].

In a study by Miedema et al., adding CAC scoring to traditional risk factors in the Multi-Ethnic Study of Atherosclerosis (MESA) cohort reclassified 20% of individuals to a higher or lower risk category [11]. Similarly, a study by Nasir et al. found that CAC scoring could help identify statin-eligible individuals who were missed by traditional risk factors [10]. Furthermore, a study by Nabi et al. used CAC scoring to risk stratify a cohort of subjects referred for invasive coronary angiography and found that the model predicted the presence of significant coronary artery stenosis and the need for revascularization [12].

South Asians (SAs) from Mediators of Atherosclerosis in South Asians Living in America (MASALA) study represent a highly educated and high-income group consistent with the immigration patterns of SAs in the US compared to Europe and Canada [13]. It is, therefore, possible that MASALA comprised a lower-risk SA subgroup compared to the studies. MASALA also excluded SAs with a history of clinical ASCVD and further excluded those on statins at baseline enriching our study population with healthy SAs. In Farjo et al. [14] study CAC ≥ 400 model to risk stratifies a cohort of 87 subjects referred for invasive coronary angiography. Using an intermediate or higher pretest probability (≥ 15%) to predict CAC ≥ 400, the model predicted the presence of significant coronary artery stenosis (P=0.025), the need for revascularization (P<0.001), notably bypass surgery.

This study goals to investigate the utility of CAC scoring in guiding treatment decisions among high-risk populations, specifically South Asians. The primary goal is to assess how CAC scoring influences cardiovascular risk reclassification and treatment decisions within a preventive cardiology clinic. We hypothesize that integrating CAC scoring into traditional risk assessment algorithms will enhance risk prediction accuracy, facilitating more precise allocation of preventive therapies, especially statin therapy, in this high-risk demographic. The study's findings have the potential to significantly influence clinical practice, addressing a critical gap in the literature and contributing to improved risk stratification and treatment decisions for South Asians at risk of CVD.

Material and Method

Study cohort

This observational cross-sectional study involved 204 consecutive, asymptomatic subjects coming for assessment at our tertiary care center's primary prevention clinic. Participants, self-referred and evaluated by specialized primary care providers, underwent a comprehensive assessment encompassing detailed history, physical examination, and laboratory evaluation. Routine Coronary Artery Calcium Scoring (CACS) was a standard part of this evaluation. All subjects were asymptomatic and free of documented cardiovascular diseases, including coronary artery disease, arrhythmic disease, peripheral arterial disease, cerebrovascular disease, aortic disease, or valvular heart disease. The study received approval from the Institutional Review Board of the hospital.

After informed consent, prior to CACS, each patient underwent structured history-taking, including a review of available medical records to establish the absence of symptoms, cardiac risk factors, past medical history, family history of premature Coronary Heart Disease (CHD), and medication use. Diabetes was identified through self-report or hypoglycemic drug usage. Hypertension was defined as untreated blood pressure exceeding 140/90 mmHg or the use of antihypertensive medication. Smoking was characterized by current or prior cigarette use. Fasting total cholesterol, high-density lipoprotein, low-density lipoprotein cholesterol, and triglycerides were assessed using enzymatic assays with an automated chemistry analyzer. Utilizing this data, the ASCVD score for each patient was calculated according to previously published formulae. The study strictly adhered to the protocols approved by the Institutional Review Board of the hospital.

Calcium scoring

The MESA methods for computed tomography scanning of coronary arteries were done to calculate CAC score. Estimates of radiation dose was determined according to the MESA protocol for a single scan obtained through the heart with the Imatron C150, Volume Zoom, and LightSpeed Pro 16 scanners is as follows: 0.6 and 0.7, 0.9 and 1.1, and 0.9 and 1.1 mSv for men and women, respectively. CAC score 0 was considered normal, while CAC score >0 was abnormal.

Statistical analysis

Continuous variables are expressed as mean ± Standard Deviation (SD), and categorical variables are reported as counts with percentage. A 10-year risk predictor score for ASCVD was calculated using baseline data according to the Pooled Cohort Equations, then categorized as low (<5%), intermediate (5 to 19.9%), and high risk (≥ 20%) group. CAC score was categorized as 0 and >0. Comparisons between CAC categories were performed by Mann-Whitney U test for continuous variables and by Pearson's χ^2 test for categorical measures. All statistical analyses were performed using IBM SPSS, version 27.0. A p value of <0.05 was considered significant.

Results

Table 1 provides a comprehensive overview of the baseline demographic and clinical characteristics of the study participants (n=204), with a majority being male (82.4%). The average age was 52 years, and the mean Body Mass Index (BMI) was 28.9 kg/m^2. A significant proportion of participants were smokers (26.5%) and had hypertension (30.9%). The average total cholesterol level was 178 mg/dl, and the mean High-Density Lipoprotein (HDL) cholesterol was 39 mg/dl. The calculated Atherosclerotic Cardiovascular Disease (ASCVD) risk and Coronary Artery Calcium (CAC) scores were 10.4 and 176, respectively.

Participants with a CAC score of 0 (108 individuals) exhibited significant differences in various characteristics compared to those

Table 1: Baseline demographic and clinical data of study participants.

		Study Sample (n=204)
Sex, n [%]	Female	36 [17.6]
	Male	168 [82.4]
Age (years), mean ± SD		52 ± 9
Height (cm), mean ± SD		168 ± 8.4
Weight (kg), mean ± SD		82 ± 15.4
Body mass index (kg/m^2), mean ± SD		28.9 ± 5.3
Smoker, n [%]		54 [26.5]
Blood Pressure (mmHg), mean ± SD	Systolic	133 ± 19
	Diastolic	79 ± 10
Treatment for hypertension, n [%]	Yes	63 [30.9]
	No	141 [69.1]
Diabetes mellitus, n [%]		67 [32.8]
Total cholesterol, mean ± SD		178 ± 45
HDL cholesterol, mean ± SD		39 ± 10
ASCVD, mean ± SD		10.4 ± 10.8
CAC, mean ± SD		176 ± 490

HDL: High Density Lipoproteins; ASCVD: Atherosclerotic Cardiovascular Disease; CAC: Coronary Artery Calcium

Table 2: Comparison of demographic and clinical characteristics based on Coronary Artery Calcium (CAC) score.

	CAC Score = 0 (n=108)	CAC Score > 0 (n=96)	*p* value
Age (years)	47 ± 7	57 ± 8	<0.001*
Male sex	86 [79.6]	82 [85.4]	0.279
Body mass index (kg/m^2)	28.7 ± 5	29.1 ± 5.6	0.667
Smoker	27 [25]	27 [28.1]	0.614
Hypertension	29 [26.9]	43 [44.8]	0.007*
Diabetes mellitus	20 [18.5]	47 [49]	<0.001*
Total cholesterol (mg/dl)	184 ± 44	172 ± 45	0.029*
HDL cholesterol (mg/dl)	38 ± 10	40 ± 10	0.107
ASCVD risk			
Low risk (<5%)	60 [55.5]	19 [19.8]	<0.001*
Intermediate risk (5-19.9%)	42 [38.9]	48 [50]	0.111
High risk (≥ 20)	6 [5.6]	29 [30.2]	<0.001*

HDL: High Density Lipoproteins; ASCVD: Atherosclerotic Cardiovascular Disease; CAC: Coronary Artery Calcium
Categorical data is presented as No. [%] and continuous data is presented as mean ± SD.
*p<0.05, Significant

with a CAC score greater than 0 (96 individuals) as shown in Table 2. Notably, individuals with a CAC score of 0 were younger (47 *vs.* 57 years, p<0.001), had a lower prevalence of hypertension (26.9% *vs.* 44.8%, p=0.007), and a lower prevalence of diabetes mellitus (18.5% *vs.* 49%, p<0.001). Additionally, participants with a CAC score of 0 had a higher total cholesterol level (184 *vs.* 172 mg/dl, p=0.029). Significant differences were also observed in ASCVD risk across these two groups, emphasizing the impact of CAC on the clinical profile.

In terms of ASCVD risk, 79 individuals fell into the low-risk category (<5%), 90 participants were classified as intermediate risk (5–19.9%), and 35 individuals were identified as high risk (≥ 20%) as shown in Figure 1. Simultaneously, participants were categorized

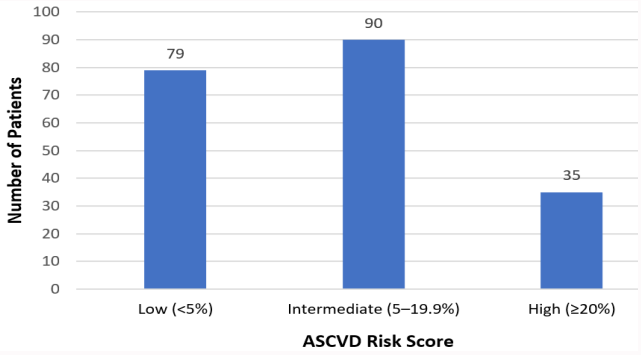

Figure 1: Distribution of study population across ASCVD risk categories. ASCVD: Atherosclerotic Cardiovascular Disease

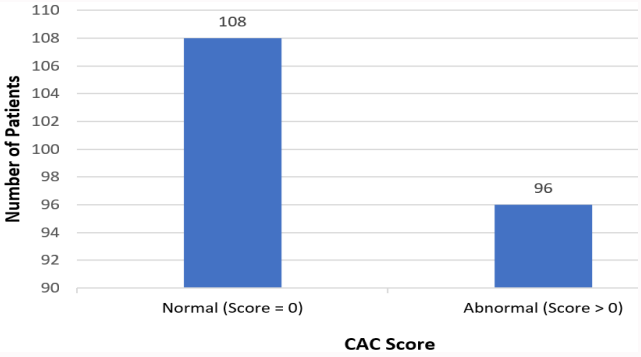

Figure 2: Distribution of study participants based on Coronary Artery Calcium (CAC) score.

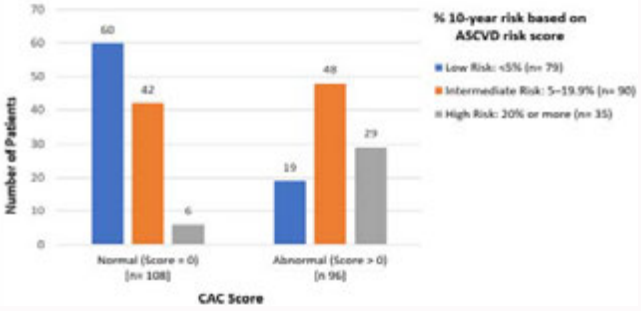

Figure 3: Redistribution of patients based on ASCVD risk and CAC score. ASCVD: Atherosclerotic Cardiovascular Disease; CAC: Coronary Artery Calcium

based on their CAC score, with 108 individuals exhibiting a normal score (0), while 96 participants presented with an abnormal score (>0) as shown in Figure 2.

Figure 3 highlights the potential reclassification of subjects when incorporating CAC scoring alongside traditional ASCVD risk assessment. A total of 71 individuals (35%) would experience a downgrade in ASCVD risk category if CAC risk categorization were applied. Among these, 42 subjects would transition from the 2nd to the 1st category, and 29 subjects would move from the 3rd to the 2nd category. Additionally, 6 individuals (3%) would undergo a 2 ASCVD risk category downgrade, specifically from the 3rd to the 1st category, resulting in a cumulative percentage of 38% within the downgraded risk category. Conversely, 19 subjects (9%) would experience a 1 ASCVD risk category upgrade, specifically transitioning from the 1st

to the 2nd category, contributing to a total of 9% of individuals with an upgraded risk category. Consequently, a noteworthy proportion, accounting for 47% of the study subjects, could potentially witness a shift in their ASCVD risk category, either through an upgrade or a downgrade, if the CAC risk categorization were applied.

Discussion

This study presents estimates of the 10-year ASCVD risk using Pooled Cohort Equation (PCE) and reclassification of this risk employing coronary artery calcium scoring in the Astro-CHARM Calculator. It is among the few conducted in South Asia. Assessing the risk of atherosclerotic cardiovascular diseases among Pakistan's numerous ethnic groups was therefore considered significant.

In our study, the pattern of ASCVD risk score was low risk in 79 (38.7%), intermediate risk in 90 (44.1%), and high risk in 35 (17.1%) patients compared to a previous cross-sectional study at the National Institute of Cardiovascular Disease, Karachi, from July 2014 to March 2015 [15]. The participants comprised male and female subjects with a multi-ethnic background, aged 20 to 79 years, and having non-atherosclerotic disease. In terms of 10-year risk, 50 males (28.2%) were projected to be at high risk, compared to 28 women (10.6%). In terms of lifetime risk, the trend in both genders was comparable in low-risk categories, 88 (50.6%) among men and 179 (68%) among women. However, lifetime risk was considerably greater in males 86 (49.4%) compared to females 84 (31.9%) in high-risk groups. Furthermore, men had greater estimates of 10-year risk in all strata, including 5.0% to 7.4%, 7.5% to 9.9%, 10.0% to 14.9%, 15.0% to 19.9%, and >20% [15].

A cross-sectional study in Pakistan collected data from 192 clinics throughout the country, encompassing both rural and urban locations. A total of 9885 individuals aged 40 to 79 years were recruited. A risk score of less than or equal to 7.5 was regarded as low danger, while a risk score of greater than 7.5 was deemed high risk. Subjects aged 50 years had a 9.73 times increased risk of higher ASCVD. Males, diabetics and smokers were more likely to have high ASCVD. Subjects with high cholesterol and using hypertension medication had a higher risk of ASCVD whereas systolic blood pressure had a substantially higher odds ratio in all ASCVD risk score [16].

Coronary Artery Calcium (CAC) is a reliable independent predictor of preclinical ASCVD and a new surrogate measure [16-19]. The growth of CAC on Computed Tomography (CT) scan has been linked to the progression and incidence of CAD, as well as mortality [20-22]. Given the high predictability, traditional risk factor-based risk assessment calculators [23] were upgraded by integrating CAC score with conventional risk factors to form a robust risk stratification modality for ASCVD [24]. The recent 2019 ACC/AHA guidelines for the primary prevention of CAD recommended ASCVD risk calculation and CAC measurement to guide statin therapy [25].

CAC scoring has been identified as a high-value care test in patients at moderate risk of ASCVD whose choice regarding statin treatment is ambiguous. CAC screening may be explored in individuals who have a greater risk than that indicated by established risk stratification techniques, including those labeled as low risk but with a family history of early ASCVD. These patients may not qualify for statins and other preventive medications based just on PCE stratification, although CAC score may further improve their categorization. Individuals with medical comorbidities that are common causes of ASCVD, such as prediabetes and Metabolic Syndrome (MetS), may also be examined for CAC scoring to assist in identifying those who may benefit from primary prevention statin and other preventive cardio-metabolic therapy.

Contrary to the MESA trial, where 41% of those recommended for statin therapy had a CAC score of zero and an ASCVD event rate of 5.2 per 1000 person-years, in our study, the coronary artery calcium score was a normal score (0 score) in 79 (54.1%) and an abnormal score (>0 score) was noted in 67 patients (45.9%) [26]. Those recommended for moderate-intensity statin treatment had a CAC score of zero in 57% of cases. The calcium score could be helpful in categorizing the patient as ineligible for statin medication [26].

In our study, when CAC risk categorization was applied, the results showed 38% individuals whose ASCVD risk category were downgraded. While 9% individuals' risk category got upgraded. In total, 47% subjects witnessed a shift in their ASCVD risk category.

From January to June 2019, the National Institute of Cardiovascular Diseases in Karachi, Pakistan, performed a study compared to the previous one. Based on the participants' mother tongues, ethnicity was classified. The Astro-CHARM Calculator and PCE were used to assess the ten-year risk of an ASCVD occurrence. According to PCE, 20.7% (80/386) and Astro-CHARM, 11.1% (43/386) of the population had high risk (7.5%) [27].

Conclusion

This study enhances the understanding of 10-year ASCVD risk assessment through coronary artery calcium scoring in a diverse Pakistani population. The findings emphasize the potential of CAC scoring to refine risk categorization, urging a personalized approach to preventive cardiology. As Pakistan addresses the growing burden of cardiovascular diseases, this research underscores the importance of personalized risk evaluation and calls for the integration of CAC scoring into evidence-based and culturally sensitive cardiovascular care strategies, aiming for a more accurate and impactful preventive approach.

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