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Original Article

Association Between Cardiovascular Risk Factors and CAD Severity by CAD-RADS Categories and Comprehensive CTA Score

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Abstract

Background: Coronary artery disease (CAD) is the leading cause of mortality and morbidity worldwide, including in Indonesia. Risk factors (RFs) play an important role in both pathogenesis and management of cardiovascular (CV) diseases. Coronary computed tomography angiography (CTA) is a reliable non-invasive diagnostic method. Coronary Artery Disease Reporting and Data System (CAD-RADS) categories and comprehensive CTA score describes CAD severity on coronary CTA and provides additional prognostic value.

Objective: To explore the link between traditional cardiovascular risk factors and CAD severity based on CAD-RADS and comprehensive CTA scores.

Methods: This retrospective, single-center study was conducted at a tertiary hospital using data from the Cardiovascular Imaging Database of the hospital from January 2020 to June 2022. Data meeting the inclusion and exclusion criteria were analyzed using ordinal and binary regressions.

Results: A total of 423 patients' data were analyzed. Ordinal regression revealed significant links between age ≥65 years, male gender, hypertension, diabetes, and higher CAD severity based on both CAD-RADS and comprehensive CTA scores. Binary regression showed that older age and male gender were independently associated with CAD-RADS ≥3 and comprehensive CTA score ≥ 6. Diabetes was linked to CAD-RADS ≥3, and hypertension was tied to a comprehensive CTA score ≥6. The number of risk factors showed a trend toward CAD severity (p=0.069) and a significant link with comprehensive CTA score (p=0.012).

Conclusion: There is a significant association between traditional cardiovascular risk factors and CAD severity as quantified by both CAD-RADS and comprehensive CTA score.

Keywords: Coronary artery disease reporting and data system, coronary computed tomography angiography, coronary artery disease severity, comprehensive computed tomography angiography score, cardiovascular risk factors

Introduction

Coronary artery disease (CAD) is a pathological process that results from the accumulation of atherosclerotic plaque in the epicardial arteries.[1] The World Health Organization (WHO) reported ischemic heart disease as the leading cause of mortality worldwide.[2] The 2021 WHO report indicated that approximately 17.9 million people died from cardiovascular diseases in 2019, accounting for 32% of all global deaths.[3] Indonesia ranks second in cardiovascular-related mortality in the region, just below Myanmar, and data from the national health insurance showed that cardiovascular disease claims cost around 9.8 trillion rupiahs (~ 640 million USD) annually.[4,5] This emphasizes the urgent need for effective

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and precise risk stratification tools to prevent major adverse cardiovascular events (MACE).

Risk factors (RFs), both modifiable and non-modifiable, play a fundamental role in the pathogenesis of cardiovascular disease. INTERHEART was the most extensive global study to characterize the risk factors associated with Myocardial Infarction (MI). A previous report demonstrated that the population attributable risk (PAR) for MI exceeds 90%, attributed to a combination of nine modifiable risk factors.[6] Additionally, older age, male gender, family history of premature CAD, hypertension, diabetes mellitus (DM), smoking, obesity, and dyslipidemia have all been well documented as traditional cardiovascular risk factors, and are frequently considered in clinical assessments. The European Society of Cardiology (ESC) recommends assessing comorbidities and conducting basic examinations (e.g., laboratory tests, ECG, echocardiography, chest x-rays, etc.) as part of the clinical method for patients with angina.[1]

Nevertheless, the focus on lumen stenosis as the primary method for quantifying CAD severity should evolve.[7] Coronary Artery Disease Reporting and Data System (CAD-RADS), introduced in 2016, aims to standardize CCTA reporting method globally. CAD-RADS are categorized from 0 to 5 based only by stenosis severity. In this context, CAD-RADS categorizes stenosis severity on a scale of 0 to 5, and higher CAD-RADS scores were associated with poorer prognosis, while CAD-RADS 0 was associated with a low cardiovascular event rate. [8,9] Other scoring systems, such as the Segment Involvement Score (SIS), Segment Stenosis Score (SSS) and the more recent comprehensive computed tomography angiography (CTA) score have been developed.[10]

Moreover, comprehensive CTA score, which was based on plaque location, type, distribution, and degree of stenosis, had been found to offer superior risk stratification compared to CAD-RADS.[11]

Cardiovascular risk factor profiles in CCTA studies vary depending on the population sampled and the quantification method used. Therefore, this study aimed to examine the association between cardiovascular risk factors and CAD severity, using CAD-RADS categories and the Comprehensive CTA Score in an Indonesian population.

Methods

This retrospective cross-sectional study utilized patient data from the Cardiovascular Imaging Database of the Cardiology and Vascular Medicine Department, Faculty of Medicine, Universitas Padjadjaran–Dr. Hasan Sadikin General Hospital, Bandung collected between January 1, 2020, and June 30, 2022.

The inclusion criteria consisted of patients with adequate CT scan image quality in all coronary artery segments. Patients presenting with acute coronary syndrome, those without traditional risk factors, individuals with incomplete CT scan reports, and those who had previously undergone percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were excluded. A total sampling method was used, in which all eligible subjects meeting the inclusion and exclusion criteria during the study period were included.

The demographic and clinical data collected included age, gender, family history of premature CAD, body mass index (BMI), hypertension history, diabetes history, smoking status, and dyslipidemia. Interpretation of the CT scans was performed by one cardiovascular imaging consultant. The definition of risk factors was based on the ACC/AHA Key Data Elements, including the definitions for Chest Pain and Acute Myocardial Infarction. Age was defined as risk factor when it was ≥65 years old. Additionally, family history of premature CAD was defined as having first-degree relatives with myocardial infarction, sudden cardiac death, CABG, or PCI who were aged <55 years for males and <65 years for females. Dyslipidemia was defined according to the NCEP-ATP III criteria, which specified total cholesterol ≥200 mg/dL, LDL ≥130 mg/dL, HDL <40 mg/dL in males and <50 mg/dL in females, triglycerides ≥175 mg/dL, lipoprotein (a) >50 mg/dL, or currently taking lipid-lowering medications. Diabetes was defined as HbA1c ≥6.5%, fasting blood glucose ≥126 mg/dL, random blood glucose ≥200 mg/dL, post-prandial blood glucose ≥200 mg/dL, or currently receiving treatment with diabetic medications. Active smoking was defined as having smoked at least 100 cigarettes during one's lifetime and reporting current smoking status.[12] Furthermore, hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or currently taking antihypertensive medication.[13] Obesity was defined as a body mass index (BMI) ≥25 kg/m^2 according to The Asia-Pacific Perspective.[14] CAD-RADS categories were established according to SCCT definitions ranging from 0 to 5.[8] Finally,

comprehensive CTA scores were calculated and categorized into 0-5, 6-20, and >20, as described in a previous study.[11]

Statistical analysis was performed using SPSS version 25.0. Categorical variables were analyzed using the chi-square test. Ordinal regression was performed to identify risk factors associated with CAD severity, followed by binary logistic regression for CAD-RADS ≥3 and Comprehensive CTA Score ≥6 to obtain odds ratios. A p-value <0.05 was considered statistically significant.

This study was approved by the Health Research Ethics Committee of the Dr. Hasan Sadikin General Hospital Bandung (approval number: LB.02.01/X.6.5/445/2022).

Results

A total of 456 patient records were available during the study period, with 33 patients meeting the exclusion criteria (i.e., 12 with severe artifacts and 21 with incomplete data). Therefore, 423 patient records were included in the final analysis. The baseline characteristics are presented in Table 1. The median age was 57 years old, most (77.1%) were categorized as elderly, and the majority of the sample were male (53.0%). Only a very small number of patients reported a family history of premature CAD (5.9%). Dyslipidemia (70.2%), obesity (57.9%), and hypertension (48.9%) were the most prevalent risk factors in the study population.

The association between risk factors and CAD severity based on CAD-RADS, assessed using ordinal regression, is presented in Table 2. The goodness-of-fit test showed that the regression model was appropriate (p value=0.158 for Pearson, 0.762 for Deviance). The model coefficient determination test achieved a pseudo-R^2 Nagelkerke score of 0.178. Older age (p<0.001), male gender (p<0.001), hypertension (p=0.039), and diabetes (0.014) were found to be variables associated with CAD severity based on CAD-RADS. Additionally, a trend of association was observed (p=0.069) between the number of risk factors and CAD-RADS categories.

Binary logistic regression findings are summarized in Table 3. The initial model for CAD-RADS had a Nagelkerke R^2 of 0.167, while the final model had a Nagelkerke R^2 of 0.158. In the final model, older age (OR 3.021, 95% CI 1.808–5.048; p<0.001), male gender (OR 3.235, 95% CI 2.122–4.930; p < 0.001), and diabetes (OR 1.914, 95% CI 1.018–3.596; p=0.044) were independent predictors of CAD-RADS ≥ 3RADS ≥ 3s associated with CAD-RADS ≥ 3.

Association between risk factors and CAD severity based on comprehensive CTA score, as determined by ordinal regression was described in Table 4. The goodness-of-fit test showed appropriate regression model (p value=0.676 for Pearson, 0.235 for Deviance). The model coefficient determination test achieved a pseudo-R^2 Nagelkerke score of 0.212. Older age (p<0.001), male gender (p<0.001), hypertension (p=0.002), and diabetes (0.034) were found to be variables associated with

Table 1 Baseline Characteristics

Variable	n= 423
Age (years)	
Median (range)	57 (18-83)
Age category	
≥65 years old	97 (22.9%)
< 65 years old	326 (77.1%)
Sex	
Male	224 (53.0%)
Female	199 (47.0%)
Family history of premature CAD	25 (5.9%)
Hypertension	207 (48.9%)
Diabetes mellitus	54 (12.8%)
Active smoker	92 (21.7%)
Dyslipidemia	297 (70.2%)
Obesity	
Body mass index (kg/cm^2), median (range)	245 (57.9%) 25.7 (15.6-61.8)
Number of risk factors	
<3 risk factors	160 (37.8%)
≥3 risk factors	263 (62.2%)
CAD-RADS	
0	85 (20.1%)
1	49 (11.6%)
2	71 (16.8%)
3	57 (13.5%)
4A/4B	124 (29.3%)
5	37 (8.7%)
Comprehensive CTA Scores	
0–5	163 (38.5%)
6–20	175 (41.4%)
>20	85 (20.1%)

Table 2 Association between Risk Factors and CAD severity based on CAD-RADS

Variable	Regression Coefficient (β)	95% CI	p-value
Simultaneous			<0.001**
Partial			
Non-modifiable risk factors			
Age ≥ 65 years old	0.878	0.450-1.306	<0.001**
Male sex	1.360	0.947-1.773	<0.001**
Family history of premature CAD	(-0.340)	(-1.083)-0.402	0.368
Modifiable risk factors			
Hypertension	0.373	0.019-0.726	0.039
Diabetes mellitus	0.660	0.145-1.305	0.013
Active smoker	0.013	(-0.461)-0.486	0.959
Dyslipidemia	0.110	(-0.272)-0.492	0.572
Obesity	0.003	(-0.348)-0.355	0.986

CAD. Furthermore, a significant association was observed (p=0.012) between the number of risk factors and comprehensive CTA score categories.

Binary logistic regression results for comprehensive CTA scores ≥ 6 are presented in Table 5. The initial model had a Nagelkerke R^2 of 0.195, while the final model had a Nagelkerke R^2 of 0.184. In the final model, older age (OR 3.278, 95% CI 1.867–5.756; p < 0.001), male gender (OR 3.747, 95% CI 2.423–5.793; p < 0.001), and hypertension (OR 1.701, 95% CI 1.015–2.618; p = 0.016) were independent predictors of a comprehensive CTA score ≥6.

Discussion

This study is the first to assess the association between traditional cardiovascular risk factors and CAD severity based on CAD-RADS categories and the comprehensive CTA score in an Indonesian population. Old age, male gender, hypertension, and DM achieved statistical significance for both types of scoring in ordinal regression. This result similar

Table 3 Binary Logistic Regression of Traditional Risk Factors with CAD-RADS ≥ 3

Variable	Initial model			Final model		
	OR	95% CI	p	OR	95% CI	p-value
Non-modifiable risk factors						
Age ≥ 65 years	3.096	1.832-5.233	<0.001	3.021	1.808-5.048	<0.001
Male sex	3.624	2.226-5.901	<0.001	3.235	2.122-4.930	<0.001
Family history of premature CAD	1.115	0.465-2.670	0.808			
Modifiable risk factors						
Hypertension	1.498	0.983-2.281	0.060	1.467	0.969-2.219	0.070
Diabetes mellitus	1.922	1.021-3.616	0.043	1.914	1.018-3.596	0.044
Active smoker	0.780	0.445-1.368	0.387			
Dyslipidemia	1.000	0.635-1.573	0.998			
Obesity	1.116	0.734-1.696	0.608			

Table 4 Association Between Risk Factors and CAD Severity Based on Comprehensive CTA Scores

Variable	Regression Coefficient (β)	95% CI	p-value
Simultaneous			<0.001**
Partial			
Non-modifiable risk factors			
Age ≥ 65 years	1.149	0.691-1.607	<0.001**
Male sex	1.394	0.948-1.840	<0.001**
Family history of premature CAD	-0.26	-1.088-0.566	0.536
Modifiable risk factors			
Hypertension	0.605	0.220-0.990	0.002
Diabetes mellitus	0.601	0.047-1.156	0.034
Active smoker	0.095	-0.405-0.595	0.710
Dyslipidemia	0.184	-0.229-0.598	0.382
Obesity	-0.183	-0.563-0.196	0.344

with previous research, which reported that old age, male gender, obesity, smoking status, and hypertension were associated with vulnerable plaque characteristics in the SCOT-HEART registry post-hoc analysis.[15] Similarly, another study demonstrated that in multivariate analysis, age greater than 45 years, hypertension, and diabetes mellitus remained significant predictors of coronary artery stenosis. A coronary artery calcium scores (CACS) categorized into zero, minimal, mild, moderate, and excessive groups showed a progressive association with significant coronary stenosis (defined as ≥50% luminal narrowing.[16]

Previous research reported that increasing

Table 5 Binary Logistic Regression Traditional Risk Factors with Comprehensive CTA Score ≥6

Variable	Initial model			Final Model		
	OR	95% CI	p	OR	95% CI	p-value
Non-modifiable risk factors						
Age ≥ 65 years	3.042	1.717-5.388	<0.001	3.278	1.867-5.756	<0.001
Male sex	3.559	2.159-5.866	<0.001	3.747	2.423-5.763	<0.001
Family history of premature CAD	0.542	0.223-1.320	0.177			
Modifiable risk factors						
Hypertension	1.728	1.114-2.678	0.015	1.701	1.105-2.618	0.016
Diabetes mellitus	1.971	0.987-3.936	0.054	1.946	0.981-3.859	0.057
Active smoker	1.023	0.555-1.883	0.943			
Dyslipidemia	0.972	0.604-1.564	0.908			
Obesity	0,857	0,554-1,325	0,487			

age was associated with higher plaque volume and burden, particularly in patients with obstructive coronary artery disease.[17] Moreover, male patients had greater plaque burden, including higher volumes of calcified, fibrotic, and lipid-rich plaques, and a higher prevalence of hemodynamically significant coronary artery stenosis compared to female patients, based on CCTA.[18] Patients with DM exhibited a higher prevalence of partially calcified plaques, non-calcified plaques, obstructive coronary artery disease, and more extensive coronary artery involvement compared to non-diabetic patients, with comorbid hypertension further increasing the risk of extensive plaque burden.[19] A previous investigation demonstrated that in symptomatic chronic coronary syndrome (CCS) patients, hypertension was associated with extensive non-obstructive coronary artery disease as assessed by coronary computed tomography angiography (CCTA), with a higher coronary segment involvement score.[20] This study showed that diabetes was an independent variable related to CAD severity based on the CAD-RADS category, which relied solely on the degree of the most severe stenosis. In contrast, hypertension was an independent variable for severity based on comprehensive CTA score that also assessed parameters such as location, number, and type of plaque, although with less stenosis.

Some risk factors were shown to have no association with CAD severity in the current study. The prevalence of family history in this study was very small (5.9%) compared to other published data, which may explain its insignificant impact.[21] Also, this study only assessed the status of active smokers and non-smokers, with a smaller prevalence (21.7%) compared to a previous study that differentiated active, former, and non-smokers. Therefore, the results of this study were likely influenced by the bias of including ex-smokers in the non-active smoker's category.[22]

Another interesting result of this study was that the results of the Nagelkerke pseudo-R^2 test (ordinal regression) and R^2 value (binary regression) were very small. The Nagelkerke R^2 and pseudo-R^2 test scores between risk factors and comprehensive CTA score were higher than those for CAD-RADS, both in ordinal and binary regression. It can be assumed that comprehensive CTA score better describes the impact of each risk factor on the development of atherosclerosis and severity of CAD. Comprehensive assessment of CTA score can provide deeper prognostic information than CAD-RADS because it assesses the relationship of risk factors to severity of CAD and detects the impact of risk factors on plaque parameters beyond stenosis, such as location, number, and type of plaque. Therefore, the additional use of comprehensive CTA score may serve as a complement to the standardized CAD-RADS report.

The present study demonstrates that traditional cardiovascular risk factors remain significantly associated with the severity of coronary artery disease in this population. Nevertheless, the retrospective and single-center nature of this study may limit the generalizability of the findings. Furthermore, several external and clinical factors including lifestyle, cultural influences, medication history, non-traditional risk factors, supporting examinations (e.g., laboratory and echocardiographic data), and validated clinical scoring—could not be evaluated due to insufficient data. Despite these limitations, the findings suggest that combining traditional cardiovascular risk assessment with CCTA-derived scoring could enhance CAD risk evaluation and guide patient management in clinical settings.

In conclusion, traditional cardiovascular risk factors specifically older age, male gender, hypertension, and diabetes mellitus are significantly associated with CAD severity based on both CAD-RADS categories and the comprehensive CTA score. These results highlight the continued importance of assessing traditional risk factors in CAD screening using CCTA.

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