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Original Research

Additional value of the coronary calcium score to conventional cardiovascular risk factors in predicting significant coronary disease diagnosed by computed tomography angiography in Angola

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Abstract: In Angola, coronary artery disease (CAD) has increased in prevalence in recent years. This study aims to evaluate the additional value of the coronary calcium score (CCS) to conventional risk factors (CRF) in predicting the presence of CAD. This study comprises 204 patients. The mean age was 56.46±9.19 years. 123(60.3%) patients are male. The patients with CAD are older (mean age 56.00±9,4 years vs. 59.83±6.8 years, p=0.017), had higher proportion of men [20(83.3%) vs. 103(57.2), p=0.014], diabetes [10(41.7%) vs. 37(20.6%), p=0.021], dyslipidemia [23(95.8%) vs. 108(60.0%], p=0.001) smoking in the past, [9(37.5%) vs 27(15.0%), p=0.007], higher number of risk factors (NRF) (p 0.001), and higher Agatston CCS (p<0.001). A logistic regression was performed to ascertain the effect age CRF, NRF, and CCS on the likelihood that participants have CAD. Based on the Backward conditional method after step 5, we identified that NFR and CCS variables added statistically significantly to the prediction (p<0.05). We identified increasing NFR (B= 0.583, Wald 5.086; OR 1.791: p=0-0024 95%CI =1.07-2.97) and CCS (B= 0.016, Wald 30.951; OR 1.016: p<0.001 95% CI =1.01-1.02) were associated with an increased likelihood of exhibiting significant CAD. Conclusion: The NRF and the CCS proved to be strong predictors of CAD.

Keywords: Coronary artery disease; Coronary calcium score; Risk factors; Computed tomography; Angola.

1. Introduction

Coronary artery disease (CAD) remains one of the main causes of morbidity and mortality worldwide for several decades [1]. It is estimated that its prevalence by 2030 will be responsible for the death of approximately 24 million people worldwide [1]. In the African continent; the trend is growing, with rates registered in a variable way depending on the country in question [2]. In Angola, malaria, tuberculosis, and AIDS are the main causes of morbidity and mortality; however, cardiovascular diseases (CVD) have been gaining ground in recent decades due to economic and social changes, as well as rapid urbanization leading to the adoption of new lifestyles and the well-known epidemiological transition [3,4].

In Angola, the broad spectrum of CVD is led by heart failure associated with hypertension dilated cardiomyopathy [5] and toxic habits deeply rooted in the population (excessive alcohol consumption) [3]. However, in recent years CAD in all its variants has increased in prevalence, which has motivated the attention of many researchers regarding this issue [3, 4, 6]. Clinically, it may present as asymptomatic myocardial ischemia, stable angina, and the so-called acute coronary syndromes (ACS), which include acute unstable angina and acute myocardial infarction [3, 5].

Coronary angiography CA is the gold standard in the diagnosis and therapeutic decision of these patients [3]. However, CA is expensive and involves a small risk of complications and death [7]. Furthermore, in Angola, up to 34.9% of patients referred for coronary angiography had normal coronary arteries and only 54.2% of patients underwent coronary revascularization [3]. Therefore, non-invasive testing is recommended to select patients who will benefit from CA. Coronary calcium is a component of atherosclerosis and a marker for the presence of coronary artery disease (CAD). Several large-scale population studies with long-term follow-ups have shown the strong predictive power of CCS for major adverse cardiac events [8]. Another major advantage of using CCS measurement lies in the fact that the non-contrast CT required for its calculation is usually associated with a much lower radiation dose than contrast-enhanced CT [8, 9]. Furthermore, computed tomography coronary angiography has shown excellent accuracy in the diagnosis of CAD when compared to conventional coronary angiography, emerging as a first-choice exam in the evaluation of patients with low to moderate pretest probability of CAD [10, 11].

The initial evaluation of a patient with suspected stable obstructive coronary artery disease (CAD) includes the clinical assessment of the pretest probability (PTP) [12]. This step is of major importance because it influences further diagnostic management [13]. This study aims to evaluate the additional value of the coronary calcium score to conventional risk factors in predicting the presence of significant coronary disease diagnosed by computed tomography angiography in patients referred for suspected CAD in Angola.

2. Materials and methods

2.1 Type and place of study

A retrospective observational cohort study was carried out, including all users who underwent computed tomography angiography of the coronary arteries at Clínica Luanda Medical Center between October 2019 and May 2022.

2.2 Study population

The study population consists of all users who underwent computed tomography angiography of the coronary arteries and who had their data included in the database at Clínica Luanda Medical Center during the referred period. Of the 233 patients who underwent cardiac CT angiography listed in the database.

2.3 Study variables

Demographic and clinical variables (cardiovascular risk factors) and coronary calcium score and severity of coronary stenosis were included. The variables were initially collected from the database at Clínica Luanda Medical Center and later from the patient's clinical files whenever necessary.

2.4 Definition of Risk Factors

Hypertension was defined based on a previous diagnosis of hypertension or treatment with antihypertensive therapy. Diabetes mellitus was defined as a previous diagnosis of diabetes mellitus, or treatment with antidiabetic drugs. Dyslipidemia was de-

fined as a previous diagnosis of dyslipidemia or treatment with any lipid-lowering medication. Obesity was defined as a BMI >30kg/m2. Smoking status was defined based on current and past smoking status (Yes/No). Alcoholic habits were defined based on the current status (Yes/No). Family history of CD was determined by the presence of a first-degree relative with a history of CD.

2.5 Coronary Calcium Score Calculation and Computed Coronary Angiography

Calculation of coronary calcium score (CCS) and computed coronary angiography was performed using a 64-slice multidetector computed tomography scanner (Somatom Perspective; Siemens, Erlagen, Germany) with the following parameters: tube voltage 100–120 kV, collimation 64 mm × 0.6 mm, and temporal resolution 0.185 s. The exams were performed with prospective electrocardiographic gating with contrast. Acquisition was performed using 3-mm slices, followed by reconstruction to a slice thickness of 0.75 mm. Images were acquired mainly at the end of inspiration and developed from the level of the carina to the base of the heart. Coronary Calcium Score was calculated following the standard methodology described by Agatston et al. [14]. Coronary stenosis was graded according to Coronary Artery Disease Reporting and Data System (CAD-RADS) as 0% (0) (no plaque or stenosis), minimal (1) <25%, 2) mild (2) 25–49.9%, moderate (3) 50–69.9%, severe (4) ≥70–99% and occluded (5) 100% [15]. All CT studies were reported by a cardiologist experienced in cardiac CT imaging, blinded to the clinical data.

2.6 Inclusion and exclusion criteria

Consecutive patients aged 18 years or older who underwent a coronary calcium score and whose sociodemographic and clinical data were collected and entered the clinic's database were included. Patients with a history of previous coronary revascularization, patients who did not undergo a coronary calcium score, patients who underwent cardiac CT angiography for an indication other than suspected coronary artery disease were excluded.

2.7 Statistical analysis

The normality of the distribution was analyzed using the Shapiro Willks test. Qualitative variables were expressed as absolute and relative frequencies. Quantitative variables were expressed as mean±standard deviation (SD) or median and interquartile range (IQR). Mann-Whitney U test, T-test for independent samples, and chi-square test were used. Statistical significance was defined as $p<0.05$. Binomial logistic regression analysis was performed with the conditional Backward method, based on the Hosmer and Lemeshow test and the Nagelkerke*R2* analysis, to predict variables of the likelihood of coronary artery disease. The analysis was performed using the Statistical Package for the Social Sciences program (SPSS, version 20.0).

3. Results

A total of 204 patients were included in the study. The mean age was 56.46±9.19 years. Of the total sample, 123(60.3%) patients are male. The most frequent cardiovascular risk factors were arterial hypertension and dyslipidemia in 75.0% and 64.2% of cases, respectively, followed by diabetes mellitus (23.0%), obesity (19.6%), and smoking in the past (17.6%). Family history of coronary disease was reported in only 8.2% of patients. Twenty-four (11.8%) patients had significant CAD. While, 180 (88.2%%) patients had no CAD, or non-significant CAD (Table 1). The median CCS of the cohort was 0(0-22). (Mean 44-6 ±117.2)

Compared to patients without CAD, the patients with CAD are older (mean age 56.00±9,4 years vs. 59.83±6.8 years, p=0.017), had higher rates of men [20(83.3%) vs. 103(57.2), p=0.014], diabetes [10(41.7%) vs. 37(20.6%), p=0.021], dyslipidemia [23(95.8%) vs. 108(60.0%], p=0.001) smoking in the past, [9(37.5%) vs 27(15.0%), p=0.007]. Further-

more, the patients with CAD had a higher number of risk factors (NRF) (p 0.001), and higher Agatston CCS (p<0.001) (Table 1). No significant difference was observed between the groups in the rate of hypertension [20(83.3%) vs. 133(73.9%), P = 0.316], smoking [2(8.3%) vs. 18(10.0%), P = 0.796] Alcoholic habits [17(70.8%) vs. 166(64.4%), P=0.537] and family history of coronary artery disease [4(16.7%) vs. 13(7.2%), P = 0.116] values.

Table 1. Demographic and clinical characteristics in the total population and according to presence of CAD.

	Total (n = 204)	**Without CAD (n =180)**	**With CAD (n = 24)**	**p-value**
Age (years)	56,41±9,18	56.00±9,4	59.83±6.8	.017*
Gender				.014*
Male, n (%)	123(60.3)	103(57.2)	20(83.3)	
Female n (%)	81(39,7%)	77(42.8)	4(16.7)	
Risk factors				
Arterial hypertension, n (%)	153 (75,0)	133(73.9)	20(83.3)	.316
Diabetes mellitus, n (%)	47 (23,0)	37(20.6)	10(41.7)	.021*
Dyslipidemia, n (%)	131 (64,2)	108(60.0)	23(95.8)	.001**
Smoking, n (%)	20 (9,8)	18(10.0)	2(8.3)	.796
Former tabagism, n	36 (17,6)	27(15.0)	9(37.5)	.007**
Obesity, n (%)	40(19,6)	33(18.3)	7(29.2)	.271
Alcoholic habits, n (%)	133 (65,2)	166(64.4)	17(70.8)	.537
Family history of CAD, n (%)	17 (8.3)	13(7.2)	4(16.7)	.116
NRF median (IQR)	3(2-4)	3(2-4)	4(3-5)	<0001***
CCS median (IQR)	0(0-22)	0(0-75)	213(85-351)	<0001***

CCS-Coronary score calcium, NRF-Number of risk factors, IQR-Interquartile range. *p<0.05;**p<0.01;***p<0.001.

A logistic regression was performed to ascertain the effect of diabetes, dyslipidemia, former smoker, age NRF, and coronary calcium score on the likelihood that participants have significant CAD. The model explained 56% (Nagelkerke R^2) of the variance in DAC and correctly classified 88,2% of cases. Based on the Backward conditional method after step 5 we identified that NFR and CCS variables added statistically significantly to the prediction (p<0.05). We identified increasing NFR (B= 0.583, Wald 5.086; OR 1.791: p=0-0024 95%CI =1.07-2.97) and CCS (B= 0.016, Wald 30.951; OR 1.016: p<0.001 95% CI =1.01-1.02) were associated with an increased likelihood of exhibiting significant CAD (Table 2)

4. Discussion

The main results of the present study revealed that, although we observed a high prevalence of cardiovascular risk factors in the studied population, only 11.8% had obstructive coronary artery disease. We also observed an association between age, male sex, diabetes mellitus, dyslipidemia, ex-smokers, number of risk factors (NRF), CCS, and significant CAD. However, in our cohort, only NRF, and CCS were independent predictors of CAD in the evaluated statistical model.

The initial evaluation of a patient with suspected stable obstructive coronary artery disease (CAD) includes the clinical assessment of the pretest probability (PTP) [12]. This

step is of major importance because it influences further diagnostic management [13]. Several scores are described for calculating the PTP of CAD. The Diamond-Forrester score (DF) was introduced in 1979 and it includes age, sex, and type of chest pain for the calculation of PTP [16]. Recently, it was updated using contemporary cohorts and extended to include patients aged>70 years [17]. This model was designated CAD Consortium 1. The Duke Clinical Score (DCS) was first described in 1983, based on a large cohort of patients referred to ICA, and it includes modifiable cardiovascular risk factors [18, 19].

Table 2. Multivariate analysis to estimate the effect of predictive variables of the presence of CHD.

Clinical variables	*B*	Wald	p-value*	OR	95% Confidence interval	
					Lower	Highest
NRF	0.583	5.086	**0.034**	1.791	1.079	2.972
CCS	0.016	30.915	**0.000**	1.016	1.010	11.913
Diabetes	0.696	0.585	0.444	2.005	0.337	1.504
Dyslipidemia	-1.869	1.917	0.166	0.134	0.011	2.174
Former Smoker	-0.556	0.504	0.478	0.573	0.124	2.662
Age	0.012	0.089	0.766	1.012	0.935	1.095

Legend.: Dependent variable: Presence of CHD. *B*.: Unstandardized Regression Coefficient. *p-value, referring to the Multiple Linear Regression analysis by the Backward: Conditional method (5º step). Significant values in bold when p<0.05. CCS - Coronary calcium score; NRF – Number of risk factors.

In a systematic review, regarding the accuracy of bedside findings for diagnosing coronary artery disease and acute myocardial infarction provided by Chun et al. the authors showed that in studies using 50% stenosis as the diagnostic standard (this cut-of was used in the present study), the pooled likelihood ratios were 5.6 for typical angina, 1.1 for atypical angina, and 0.1 for nonanginal chest pain. In turn, the pooled likelihood ratios for hypertension, diabetes, smoking, moderate hypercholesterolemia, family history of coronary artery disease, and obesity were each 2.3 or less, meaning that the presence of any of these risk factors shifted the probability of disease very little. Even combinations of risk factors increased the probability of disease by only a small amount [20].

The study by Genders et al, a retrospective pooled analysis, and the study by Budoff et al., showed that coronary artery calcium score provides had an incremental predictive power in pretest clinical probability (PTP) assessments of the extent and severity of angiographically significant CAD in symptomatic patients [21, 22]. This is in line with the findings found in our study. The strength of the association of risk factors with coronary artery disease is not fully understood. Although we found a high prevalence of cardiovascular risk factors in our cohort the prevalence of CAD was low. Genetic factors and ethnicity will certainly play an important role in the development of CAD [23, 24].

We did not evaluate the characteristics of chest pain in our patients, which did not allow us to include it in the analysis model of CAD predictors, constituting one of the main limitations of the study. Another limitation was the impossibility of comparing the findings of coronary CT angiography with conventional coronary angiography.

5. Conclusion

Our results revealed a high prevalence of cardiovascular risk factors in our cohort. Despite this, the prevalence of CAD was low. The number of risk factors and the coronary calcium score proved to be strong predictors of CAD. We believe that prospective studies are essential to evaluate the best model of scores (using simultaneously chest pain

characteristics, cardiovascular risk factors, and coronary calcium score) for calculating the pretest probability of coronary artery disease in our population.

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Research Ethics Committee Approval: The study was approved by the Directorate of Clinic Luanda Medical Center under the direction of the Center for Advanced Studies in Medical Education and Training at Agostinho Neto University. The preservation and confidentiality of patient information were guaranteed, following all standards for research on human beings following the Declaration of Helsinki on ethical principles for research on human beings.

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Conflicts of Interest: The authors declare no conflict of interest.

Supplementary Materials: None.

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