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Health Review

Prevalence of coronary artery stenosis on computed tomography angiography of the coronary arteries in stable patients with zero coronary calcium score in Angola

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Abstract: Coronary artery calcium is a component of atherosclerosis and a marker for the presence of coronary artery disease (CAD). It can be quantified based on non-contrast computed tomography (CT) using coronary calcium score (CCS) according to the Agatston method. This study aimed to assess the prevalence of CAD in a population with a zero CCS, using 64-slice CT in Angola. A total of 204 patients were included in the study. Of the total sample, 60.3% of the patients were male. The mean age was 56.46±9.19 years. The mean CCS of the cohort was 44.4±117(range, 0–889). Among 204 patients, CCS was zero in 136 (66.7%) patients, and 68 (33.3%) patients had a CCS ≥1. Compared to CCS ≥1, patients with CCS=0 were younger (age 54.7±9.3 years vs. 59.9±7.9 years, p <0.001) and the proportion of women was significantly higher (47.1% vs. 25.0%, p 0.002). Patients with CCS zero had also less history of diabetes mellitus, dyslipidemia, and smoking in the past. Of the 136 patients with CCS=0, one (0.7%) had obstructive CAD, and 16 (11.8%) had non-obstructive CAD. Our results suggest that the absence of calcium was associated with a very low probability of significant stenosis of the coronary arteries.

Keywords: Coronary calcification; Coronary artery disease; Computed tomography angiography; Angola.

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1. Introduction

The presence of coronary artery calcium (CAC) is a well-known marker of atherosclerotic disease [1]. Coronary artery calcification can be quantified based on non-contrast computed tomography (CT) and is quantified using coronary calcium score (CCS) according to the Agatston method. 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 [2]. Furthermore, 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 [2, 3].

Although several studies have shown that a CCS with a score of zero is associated with a very low prevalence of significant coronary artery stenosis in symptomatic and asymptomatic cohorts [3-7], others have reported a moderate to the high prevalence of significant coronary stenosis in patients with a CCS zero on CT [8-10]. These studies differed widely in terms of scanner type, racial differences, and risk profile [3].

The present study is the second part of a study on the importance of computed tomography (CT) angiography of the coronary arteries in the evaluation of patients with suspected coronary artery disease (CAD) in Angola. The first part aimed to evaluate the additional value of the CCS to conventional risk factors in predicting the presence of significant coronary disease diagnosed by CT angiography in patients referred for suspected CAD [11]. This second part, aims to assess the prevalence of CAD in a population of stable patients with a zero CCS, using 64-slice CT.

2. Methodology

The methodology has been described in detail elsewhere [11]. Briefly, a cross-sectional descriptive observational study was carried out in a single diagnostic center in Luanda, Angola. We recruited individuals who were referred to our center to perform computed tomography (CT) angiography of coronary arteries between October 2019 and May 2022.

The study included 204 healthy individuals aged 18 years or older who fulfilled the inclusion criteria and agreed to participate in the study. Age, sex, and the presence or absence of cardiovascular risk factors was recorded. Patients with a history of previous coronary revascularization, patients who did not undergo coronary calcium score (CCS), patients who underwent cardiac CT angiography for an indication other than suspected coronary artery disease were excluded.

Calculation of 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. The dataset was divided into two groups according to the coronary calcium score in group I-CCS = 0 and group II-CCS ≥1. CCS was calculated following the standard methodology described by Agatston et al. [12]. 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% [13]. All CT studies were reported by a cardiologist experienced in cardiac CT imaging, blinded to the clinical data.

Lastly, we performed a search on Pubmed, using the keywords "*prevalence of coronary disease in patients with coronary calcium*" and "*multislice computed tomography*". Nine of the 73 articles that returned were related to the objectives of our study and were included in the literature review.

2.1 Statistical analysis

The normality of the distribution was analyzed using the Shapiro Wilk 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 $p<0.05$. The analysis was performed using the Statistical Package for the Social Sciences program (SPSS, version 20.0).

3. Results

3.1 Demographics characteristics

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 were male (Table 1).

Table 1. Demographic and CT angiography findings in the total population and according to coronary calcium score = 0 or ≥1.

Variables	Total (n = 204)	CCS =0 (n =136)	CCS ≥1 (n = 68)	p-value
Age	56,41±9,18	54.68±9.33	59.88±7.86	<0.001
Gender				0.002**
Male, n (%)	123(60.3)	72(52.9)	51(75,0)	
Female n (%)	81(39,7%)	64(47.1)	17(25.0)	
Coronary artery disease				<0.001***
Significant coronary artery disease n (%)	24(11,8)	1(0.7)	23(33.8)	
Non-obstructive coronary artery disease n (%)	60(29.4)	16(11.8)	44(64.7)	
No coronary disease n (%)	120(58,8)	119(87.5)	1(1.5)	
Number of vessels affected (any plaque)				<0.001***¥
Left main disease n (%)	7(3,5)	2(1.5)	5(7.4)	
1-vessel disease n (%)	46(22,5)	11(8.1)	35(51.5)	
2-vessel disease n (%)	19(9.3)	3(2.2)	16(23.5)	
3-vessel disease n (%)	12(5.9)	1(0.7)	11(16.2)	
No atherosclerotic lesions	120(58,8)	119(87.5)	1(1.5)	
Number of vessels affected (stenosis >50%)				-
Left main disease n (%)	2(0.98)	0(0.0)	2(2.9)	
1 vessel disease n (%)	12(5.9)	1(0.7)	11(16.2)	
2 vessel disease n (%)	7(3.4)	0(0.0)	7 (10.3)	
3 vessel disease n (%)	3(1.5)	0(0.0)	3(4.4)	
No atherosclerotic or significant lesions	180(88.2)	135(99.3)	45(66.2)	

¥-Fisher's exact test. *p<0.05, **p<0.01, ***p<0.001.

3.2 CT coronary angiography findings

The mean CCS of the cohort was 44.4±117(range, 0–889). Among 204 patients, CCS was zero in 136 (66.7%) patients, and 68 (33.3%) patients had a CCS ≥1. One hundred twenty (58.8%) patients had no CAD, 60 (29.4%) patients had non-obstructive CAD and 24 (11.8%) patients had significant CAD. Concerning the presence of any atherosclerotic plaque, 3.5% of the patients had left main coronary artery disease, 22.5% had a 1-vessel disease, 9.3% had a 2-vessel disease, and 5,9% had a 3-vessel disease. Regarding patients only with coronary stenoses >50%, the percentages were 0.98, 5.9, 3.4, and 1.5%, respectively (Table 1).

The type of plaques found in 16 (42.9%) patients with CCS zero and non-obstructive CAD are shown in table 2. Of the 21 plaques observed, 9 (42.9%) were fibrolipidic and 12 (57.1%) were mixed plaques. Furthermore, 81.0% of all plaques had coronary artery stenosis <25%. The only patient with obstructive CAD and CCS=0 had a single stenotic lesion >70% in the left anterior descending artery (Figure 1). In turn, a patient with CCS of 134.6 had a severe stenotic lesion in the proximal and middle segments of the LAD (Figure 2).

3.3 Comparison analysis

Compared to CCS ≥1, patients with CCS = 0 were younger (mean age 54.7±9.3 years vs. 59.9±7.9 years, p <0.001), and the proportion of women was significantly higher (47.1% vs. 25.0%, p<0.01) (Table 1). Patients with CCS zero had also less history of diabetes mellitus, dyslipidemia, and smoking in the past (14.3% vs 39.7% p<0-001; 57.4 vs

77,9 p<0-01; 13.2% vs 26.5% p<0.05, respectively). Furthermore, our results showed an association between CCS and CAD. Compared to SCC = 0, patients with SCC ≥1 have a higher percentage of patients with significant CAD and non-obstructive CAD (33.8% and 64.7% vs 1,5%; p<0.001, respectively) (Table 1).

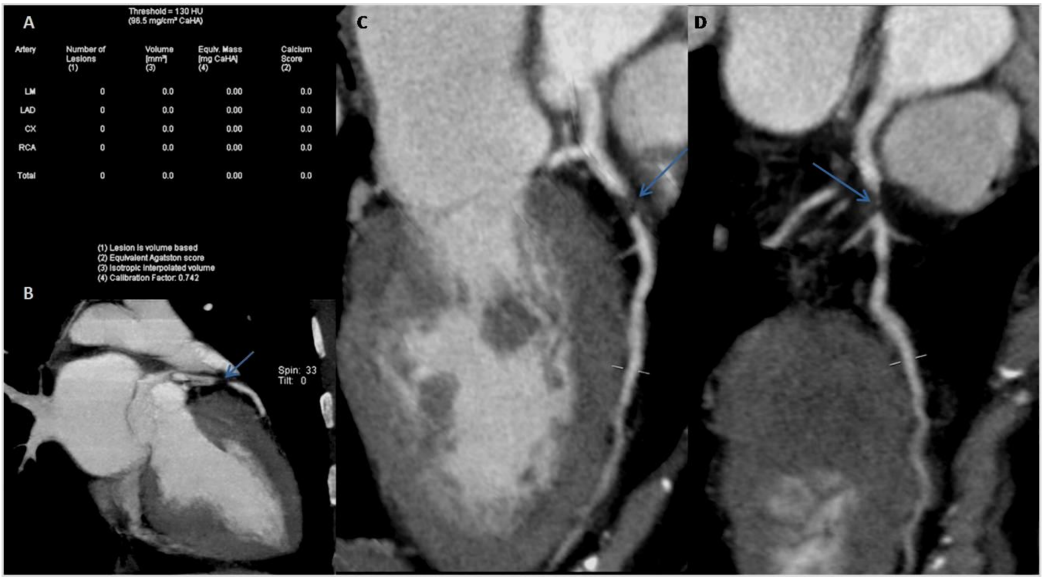

Figure 1. A. 53-years old black male with CCS=0. **B.** Soft plaque which causes severe stenosis (>90%) is seen in proximal segment of LAD (arrow); Sagital view (B). **C and D.** MIP curved multi-planar reformate.

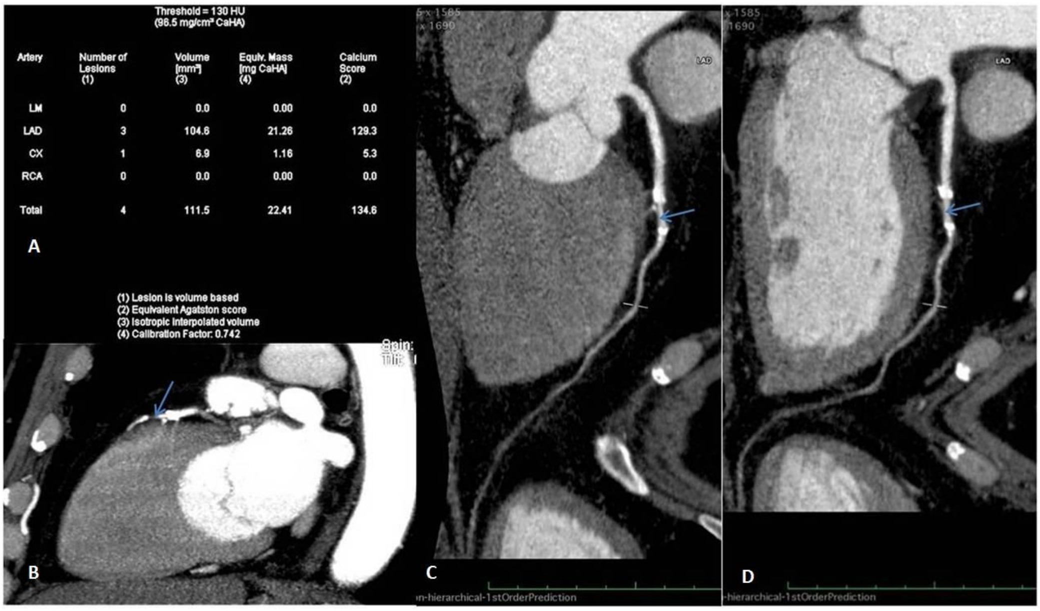

Figure 2. A. A 68-years old caucasian male with a total CCS=134.6 with calcified plaques in the proximal and middle segments of LAD. **B.** A severe stenosis (>70%) is seen in proximal and middle segment of LAD (arrow); Sagital view. **C, D.** MIP curved multiplanar reformate.

The prevalence of non-obstructive and significant CAD, as well as the absence of CAD according to SCC=0 vs CCS≥1, is shown in Figure 3. There was a significant increase in severity of CAD related to increasing CCS. However, we would like to point out that of the 136 patients with zero-CCS, one (0.7%) patient had obstructive CAD and 16 (11.8%) patients had non-obstructive CAD.

Table 2. Type of atherosclerotic plaques, degree of stenosis and coronary artery distribution in patients with coronary calcium score zero and non-obstructive coronary artery disease (n – 16).

	Left main	**Left anterior descending artery**	**Left circumflex artery**	**Right coronary artery**	**Total**
Type of atheromatous plaque					
Fibrolipid plaque, n (%)	2 (28.6)	3 (37.5)	1 (50.0)	3 (75.0)	9 (42.9)
Mixed plaque, n (%)	5 (71.4)	5 (62.5)	1 (50.0)	1(25.0)	12 (57.1)
Total n (%)	7 (100)	8 (100.0)	2 (100.0)	4 (100)	21 (100.0)
Degree of coronary artery stenosis					
<25%, n (%)	6 (85.7)	5 (62.5)	2 (100.0)	4 (100.0)	17 (81.0)
25-50%, n (%)	1 (14.3)	3 (37.5)	0 (0.0)	0 (0.0)	4 (19.0)
Total n (%)	7 (100)	8 (100.0)	2 (100.0)	4 (100.0)	21 (100.0)

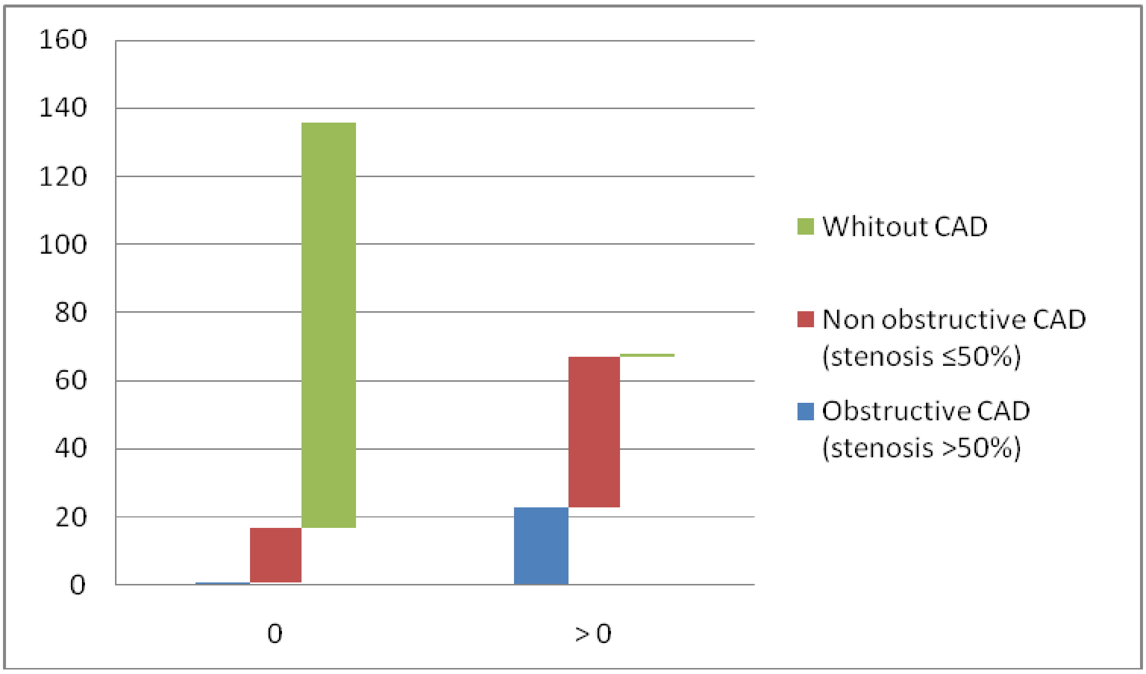

Figure 3. Distribution of coronary artery disease (CAD) according to coronary calcium score = 0 vs >0 (Agatston Units).

3.4 Studies that evaluated the prevalence of obstructive CAD in patients with CCS equal to zero using 64-slice MDCT.

The results of the 9 published studies that evaluated the prevalence of significant CAD in patients with a CCS equal to zero, using the 64-section CT, are shown in Table 3. We found that the prevalence of significant CAD varied between 3,1% and 19,4% depending on the population studied.

4. Discussion

The prevalence and clinical significance of CAD obstruction on coronary CT angiography in patients with zero CCS have been evaluated in several cohorts, but with conflicting results, depending on the population included. Results on the prevalence of obstructive and non-obstructive CAD in studies carried out in stable patients using 64-slice CT are presented in table 3. The prevalence of obstructive CAD varied between 3.1 and 19.4% and non-obstructive CAD between 8.4 and 16,2% [5-7,14-18].

Table 3. Diagnostic value of CCS 0 in stable chest pain patients using 64-slice MDCT.

First author (year)	**Population (N, % men, mean age ± SD)**	**CT system**	**cCTA ≥ 50 % luminal stenosis N (%)**	**Total number of patients with a CCS 0 n (%*)**	**Total number of CCS 0 patients with OCAD n (%)**	**Total number of CCS 0 patients with non-OCAD n (%)**
Low pretest probability of coronary disease						
Kwon (2011) [5]	N = 3979, 44 % men Age: 60 ± 10	64-slice MDCT	622 (16)	2406 (61)	90 (3.7)	n. r.
Nicoll (2016) [16]	N = 5515, 61 % men Age: 60 ± 12	64-slice MDCT	1538 (28)	1987 (34)	109 (5.5)	n. r.
Low to moderate pretest probability of coronary disease						
van Werkhoven (2009) [15]	N = 432, 58 % men Age: 58 ± 11	64-slice DCT	109 (25)	117 (34)	5 (4,3)	19 (16,2)
van Werkhoven (2010) [18]	N = 576, 47 % men Age: 56 ± 12	64-slice MDCT	168 (29)	242 (42)	14 (5.8)	n. r.
Villines (2011) [7]	N = 10 037, 56 % men Age: 57 ± 11	64-slice MDCT	2069 (21)	5128 (51)	180 (3.5)	667 (13)
Kim (2012) [6]	N = 2088, 49 % men Age: 59 ± 10	64-slice MDCT	444 (21)	1114 (53)	48 (4.3)	n. r.
Bom (2016) [14]	N = 1551, 38 % men Age: 58 ± 10	64-slice MDCT	214 (14)	739 (48)	23 (3.1)	62 (8.4)
Moderate and high pretest probability of coronary disease						
Gottlieb (2010) [9]	N = 291, 73 % men Age: 59 ± 10	64-slice MDCT	163 (56)	72 (25)	14 (19)	n. r
Pre-test probability of coronary disease, not reported						
Akram (2009) [17]	N = 210, 47 % men Age: 57 ± 11.8	64-slice MDCT	28 (21)	70 (34)	4 (5.7)	n. r.
Present series	N = 204,60.3 % men Age: 56,41±9,18	64-slice MDCT	25 (12)	136 (67)	1(0.7)	16 (11.8)

CCS – Coronary calcium score, CT - Computed tomography cCTA – Coronary computed tomography angiography, MDCT – Multidetector computed tomography, OCAD – Obstructive coronary artery disease.

The prevalence of moderate to severe CAD found in our cohort was slightly lower than that found in the CONFIRM Registry [7], and in the studies, Bom et al. [14] Kwon et al [5], Kim et al [6], van Werkhoven et al. [15], Nicoll et al. [16], Akram et al. [17], and van Werkhoven et al. [18], (3.5, 3.1, 3.7, 4.3, 4.3, 5.5, 5.7, and 5,8% respectively). Furthermore, the prevalence of non-occlusive atherosclerotic lesions found in the CONFIRM Registry and in the study by Bom et al. [14], (13% and 8.4%, respectively) are very similar to those found by us. This may be explained by a high prevalence of patients with low [7], and low to moderate pretest probability of CAD.

Furthermore, the study by Akram et al. [17] showed that the prevalence of obstructive CAD in patients with zero CCS was 8% and 0% in symptomatic and asymptomatic patients respectively, showing the impact of the type of population studied in the prevalence of obstructive CAD [17].

In turn, in the study by Gottlieb et al. [9], there was a high prevalence of obstructive CAD in patients with CCS zero (19%,), which may be related to the fact that patients with moderate to the high probability of coronary disease were included in this study. van Werkhoven et al. [15], in turn, found a prevalence of non-obstructive CAD in patients with SCC zero of 16.2%.

The CCS allows non-invasive quantification of the total coronary atherosclerotic burden, although it underestimates the burden of disease, as it does not measure non-calcified plaques [19]. Data from the present study corroborate this statement, 17 of the 137 patients with CCS=0 had CAD. (1 occlusive CAD and 16 non-occlusive CAD), with mixed and fibrolipidic plaques. Despite this, the CCS has proven to be superior to traditional risks stratification tools, such as clinical risk factor assessment, ankle-brachial index, carotid intima-media thickness, and high-sensitivity C-reactive protein, as a predictor of cardiovascular events [20, 21]. Studies that evaluated the prognostic value of SCC revealed that patients with SCC=zero have a good prognosis (especially those without atherosclerotic lesions and those with stenoses <50%) [6, 7, 17, 22, 23], it is a group that is unlikely to derive short-term benefit from risk-reducing pharmacotherapy [23].

Data related to a higher prevalence of male patients, younger patients with less history of diabetes mellitus, dyslipidemia, and past smoking, in the group with SCC=0 when compared to the group with SCC>0 found in our cohort, are like those found in other cohorts in the vast majority of studies [7, 14,22,24,25] but not in all [26]. Contrary to our results, Feuchtner et al. [26] found a lower prevalence of arterial hypertension in the group with CCS=0 when compared to the group with CCS≥1. Furthermore, regarding other risk factors, except diabetes mellitus, they did not find differences between the two groups regarding age, sex, and prevalence of dyslipidemia [26].

5. Limitations

The present study is limited by a) the small sample size of 204 patients, b) the lack of patient follow-up; c) the correlation of CTA findings with conventional angiography was not possible.

6. Conclusions

Our results suggest that patients with zero coronary calcium score had a low prevalence of significant coronary artery disease. On the other hand, the absence of calcium does not exclude the presence of non-obstructive atherosclerotic lesions that may eventually be the object of primary prevention. In this context, it is suggested that longitudinal studies be carried out to assess the prognostic value of the coronary calcium score in this population in Angola.

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Research Ethics Committee Approval: The study was approved by the Directorate of Clínica 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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Supplementary Materials: None.

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