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Research Article

The Assessment of Severity in Patients with Coronary Artery Disease Through Coronary Angiotomography and Physical-Functional Assessment

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Abstract

Background: The assessment of the coronary artery calcium score and the degree of coronary stenosis with the aim of tracking a higher risk for coronary events, when associated with an assessment of functional health, may indicate possible physical disabilities that will impact their quality of life.
Design: Cross-sectional study.
Methods: 208 patients underwent coronary artery calcium score quantification and were divided into absent (0), low (1-100), intermediate (101-400) and high / very high (> 400), as well as the degree of coronary artery stenosis through percentage. Functional assessment was performed through the measure of functional independence, modified Katz index and Barthel index, and for physical capacity and the 6-minute walk test, with statistical analysis through analysis of variance.
Results: The middle ages were 57±11,2 years and 61,5% were females. The most frequent risk factors were high blood pressure (78,4%) and family history to CAD (72,1%). The most common level was intermediate, 23,8%. The functionality showed a deficit of 19%; the distance travelled was 67,9% of the predicted distance, with differences observed between coronary arterial calcium score groups (p=0,03). The functionality was associated with the sedentary lifestyle (p=0,007) and dyspnea (p=0,008), while the physical capacity was associated with the dyspnea (p=0,03).
Conclusions: Patients with coronary artery disease with a higher calcium score (>400) had reduced physical capacity. Functionality showed that there was an association with a sedentary lifestyle and dyspnea.

Key words: coronary artery disease; exercise test; computed tomography angiography; coronary stenosis; functional assessment

1. Introduction:

Cardiovascular disease is the leading cause of global mortality. Studies show that approximately 17.5 million deaths are caused by cardiovascular disease worldwide, of which approximately 7.5 million are due to atherosclerosis, and in Brazil it accounts for 30.4% of the total number of deaths [1,2,3].

Diagnosing coronary artery disease (CAD) is important not only with respect to disease state but also to assess its impact on the functional activities of daily life (ADL). Measurement of quality of treatment includes how well the function is restored in terms of mobility in relation

to daily activities, exercise, and quality of life as well as preventing functional incapacity [4].

Therefore, health must be measured not only by the presence or absence of disease but also by the degree to which it affects functional capacity and the capacity to carry out ADL. Therapy can be considered to be successful when the autonomy of an individual is maintained and he/she can continue his/her normal social interactions [5,6]. Heart disease represents a biophysical imbalance because it is also associated with a social/mental impact [7,8].

In addition to evaluating coronary arterial calcium score (CACS) and the stenosis arterial, and the analyzing functional independence in cardiac patients should be considered as an indicator of the success of treatment and the prognosis of morbidity and mortality [6].

Coronary computed tomography angiography (CCTA) is a method for evaluating symptomatic patients and its function is to identify whether or not there are significant obstructive lesions that justify the symptoms. These two techniques are routinely used in clinical cardiological evaluations and are employed to detect and quantify coronary calcification and assess the presence of stenosis [7,8].

This study aimed to evaluate the association between CACS and coronary stenosis with functionality and the physical capacity of patients with suspected CAD. This would allow patients with CAD to set appropriate limits for physical effort to try to maintain activities of daily living at an optimum level.

2. Materials and Methods

This was a cross-sectional study on consecutive patients with CAD of both genders under clinical investigation. Participants comprised patients referred by their cardiologists for CCTA. During the initial evaluation of the patient, the likelihood of CAD was assessed according to the score calculated using the Diamond–Forrester algorithm [12]. Data were collected in a public hospital and other private service providing CCTA (Toshiba Aquilion and GE Healthcare VCT), in Aracaju, Brasil. The study was approved by the research ethics committee of the Federal University of Sergipe under protocol 0289.0.107.000-11. Following CCTA, patients were divided into four groups according to their CACS: absent, 0; low, 1–100; intermediate, 101–400; and high/very high, >400.

Inclusion criteria [3,7] for the study were as follows: patients of both sexes with suspected CAD, agreement to participate in the study, and the capacity to understand and sign the informed consent and answer the questions in the instruments. The exclusion criteria [3,7] were as follows: clinically unstable patients; refusal to participate in the study; patients with cerebrovascular diseases associated with motor sequelae; a known allergy to iodinated contrast medium; nephropathy; a history of multiple myeloma or organ transplant; a high serum creatinine level (>1.5 mg/dL); clearance of calculated creatinine < 60 mL/min; and a known or suspected intolerance or contraindication to beta blockers including allergic reactions, lung disease with bronchospasm in addition to any illness on the day of assessment, such as cold, flu, or fever that could affect the physical capacity test. In total, 208 patients were referred for evaluation.

208 patients, users of the cardiology service, were randomly those who completed the CACS and the assessment of functionality. Of these, 164 patients underwent only the assessment of the coronary arterial calcium score.

Functionality was assessed using the Functional Independence Measure (FIM), and activity levels of daily living (ADL) were assessed using the Barthel scale and the modified Katz index. In addition to these instruments, the 6-minute walk test (6MWT) was used as a marker for physical capacity [4,5,12].

Categorical variables studied were divided into general characteristics [3,5,6]: age, gender, weight, body mass index (BMI); life habits: smoking, alcohol use and physical activity; risk factors: high blood pressure, diabetes mellitus, dyslipidemia, obesity, and family history of CAD; and symptoms: typical and atypical precordialgia, dyspnea, and CAD. The outcome variables were as follows: FIM, Barthel index, modified Katz index, distance traveled in meters in 6MWT, percentage of predicted distance achieved, CACS (absolute values), coronary stenosis (%), and the number of arteries affected.

The FIM scale is broad in scope and its validity is accepted in the international literature. It is easy to implement and understand, and assesses motor and cognitive components in various clinical conditions. Furthermore, it is considered a measure that meets the criteria of reliability, validity and precision [9].

The Barthel index also measures functional independence in relation to personal care, mobility, locomotion, and bowel and bladder function. The version used in this study evaluated functional independence in 10 tasks: feeding, bathing, dressing, grooming, bowel elimination, bladder eliminations, toilet, chair/bed transfers, walking, and stairs. Patients who required assistance from another person in any of the tasks were considered to be “dependent” [10].

The modified Katz index was used because it evaluates independence in terms of ADL when accomplishing activities without supervision or any kind of direct guidance. The index indicates the ability of the patient to have an independent life. This instrument assesses functionality in six areas (bathing, dressing, going to the bathroom, bed/chair transfer, continence, and feeding) [11].

Physical capacity was assessed by the ability to walk and was assessed by the distance covered in meters during the 6MWT, being performed according to the recommendations of the American Thoracic Society [12]. The predicted distance was calculated according to individual characteristics and anthropometric parameters for the Brazilian population [13].

Coronary arterial calcium score (CACS) was calculated using Coronary Tomography Angiography (CCTA). Coronary artery calcification was defined as regions of the arteries with density >130 Hounsfield units (HU), as described by Agatston [14]. The sum of the calcium present in each coronary artery and its derivatives gives the total value and CACS and quantified in Agatston units (AU), as follows: absence (0 AU), low (1–100 AU), intermediate (101–400 AU), high (401–1000) or very high (> 1000 AU). For coronary stenosis, they were considered obstructive when >50% of the light was obstructed, being classified as low when the reduction was <50% of the light.

Statistical Analysis

The Shapiro-Wilk test was used to assess the normality assumption, with a result for the normality of the sample. The chi-square test for hypotheses about categorical variables. Categorical variables are presented as: CACS groups, sex, alcohol, smoking, physical activity, hypertension, obesity, diabetes, hypertension, dyslipidemia, family history, asymptomatic, dyspnea, typical and atypical precordialgia, and history of CAD. While

the variables are continuous in the study, the functional variables of FIM, KATZ and Barthel, and the distance covered and predicted.

For comparison between the CACS groups, One-way ANOVA was used if there was a statistically significant difference between the groups compared, followed by Tukey's test. To analyze the mean, Student's t-test, unpaired test, or Mann-Whitney test was used to compare means of the distance walked and the predicted distance between calcium score groups. The level of significance adopted was $p \leq 0.05$ (95%) and the analyzes were performed using the SPSS program, version 21.0.

While to analyze the variables in relation to the distance covered, a general linear model was used for the dependent function variables and the fixed factors of sedentary lifestyle, dyspnea, CACS categories and degree of stenosis. Analysis of associations between functional dependence and factors such as age, gender, sedentary lifestyle, dyspnea, diabetes mellitus, hypertension, degree of CACS (absent, low, intermediate and high / very high) and degree of stenosis (absent, < 50% and > 50%) were performed using "backward" logistic regression.

3. Results

The sample consisted of 208 patients with an average age of 57±11,2 years, with a higher frequency of females (61,5%). With respect to lifestyle, only 39,5% reported including regular physical activity, whereas alcohol use and smoking presented similar frequencies (Table 1).

VARIABLES	TOTAL (n=208) (%)
Age (years) [1]	57 ± 11,2
Female gender	128 (61,5)
Weight (kg) [1]	72,9 ± 16
Body mass index[1]	28 ± 5,6
Alcohol use	67 (32,7)
Smoking	54 (26,3)
Physical activity	77 (39,5)
High blood pressure	160 (78,4)
Obesity	74 (36,5)
Diabetes mellitus	61 (29,9)
Dyslipidemia	119 (58)
Family history	137 (72,1)
Asymptomatic	47 (23)
Dyspnea	70 (34,5)
Precordialgia typical	80 (39)
Precordialgia atypical	74 (26,1)
CAD history[2]	20 (9,9)

[1]Values expressed as mean ± standard deviation. Other values expressed in absolute value (n) and relative frequency (%) CAD = coronary artery disease. Some patients have more than one of the symptoms (dyspnea, atypical pain and pain). [2] Previous acute myocardial infarction was considered as prior history of disease.

Table 1: General and clinical characteristics of patients with CAD.

The proportion of patients with CACS of >0 was 49,5% [95% confidence interval (95% CI) 42,7–56,3], 23,8% patients had CACS of 1–100, 16,5% patients had CACS of 101–400, and 9,2% patients had CACS of >400 (Table 2).

CORONARY ARTERY CALCIUM SCORE (CACS)	TOTAL (N=206)	RELATIVE FREQUENCY (%)1	CI 95%2	RR3
HIGH/VERY HIGH (CACS > 400)	19	9.2	5.8-13.6	7,2
INTERMEDIATE (CACS 101-400)	34	16.5	11.7-22.3	4,3
LOW (CACS 1-100)	49	23.8	18.0-30.1	1,9
ABSENT (CACS = 0)	104	50.5	43.7-57.3	

[1]Values expressed in n and percentage (%) of patients. [2]CI 95%: confidence interval estimated by Bootstrap technique. [3] Relative Risk (RR) according to the II MRI Directive and computed tomography Brazilian society of Cardiology cardiovascular and Brazilian College of Radiology,2014.

Table 2: CACS distribution score in patients.

Of the 208 patients, CCTA was performed on 164 patients. The degree of stenosis and number of affected arteries were as follows: 44% showed an absence of stenosis, and 33% had coronary stenosis obstructive (>50%). Furthermore, 44% patients had no affected arteries, 18% had single-artery

involvement, 26% had involvement in two arteries, and 11% had involvement of ≥3 arteries (Table 3).

Degree of Stenosis	Total (N=164)	Relative Frequency (%)	CI 95%	Number of Arteries Affected	Total (N=164)	Relative Frequency (%)	CI 95%
0	73	44	69.8-77.4	0	73	44	69.8-77.4
1-49 %	36	22	61.4-73.6	1	30	18	65.5-77
> 50%	55	33	58.3-69.3	2	43	26	57-70
				3+	18	11	49.7-69.4

Table 3: Angiotomographic data in patients.

Assessment of functionality according to distance walked showed that only 67,9% of the patients reached the expected distance in the 6MWT, (average of 368,2 meters of an expected average of 534,9 meters). FIM showed mean values of Katz and Barthel indicating functional independence.

With respect to age and categories of CACS according to the degree of calcification, a significant association (p=0,0499) was observed. Patients in the CACS>400 group were significantly older (mean=6,5 years, 95% CI 55,6–58,7) than those in the other CACS groups (Table 4).

CLINICAL CHARACTERISTICS	CACS=0 (N=104)	CACS=1-100 (N=49)	CACS=101-400 (N=34)	CACS>400 (N=19)	p
Age[1]	53.4 ± 11.6	59.9 ± 8.3	59.8 ± 9.3	65.9 ± 11.0	0.05
Female	67 (64.4)	30 (61.2)	22 (64.7)	7 (36.8)	0.146
Male	37 (35.6)	19 (38.8)	12 (35.3)	12 (63.2)	
BMI[1]	27.9 ± 5.6	29.5 ± 5.9	27.3 ± 5.9	26.8 ± 4.2	0.638
Smoking	21 (20.6)	11 (22.9)	14 (41.2)	8 (42.1)	0.041
Alcohol use	36 (35.3)	17 (35.4)	10 (29.4)	4 (21.1)	0.616
Physical Activity	39 (40.2)	18 (39.1)	13 (38.2)	7 (38.9)	0.534
Obesity	33 (32.4)	24 (51.1)	11 (33.3)	6 (31.6)	0.147
High blood pressure	78 (74.3)	40 (79.6)	28 (87.5)	17 (94.1)	0.160
Diabetes mellitus	19 (18.6)	16 (33.3)	17 (50)	8 (42.1)	0.002
Dyslipidemia	47 (46.1)	34 (70.8)	23 (67.6)	13 (68.4)	0.01
Family history	66 (70.2)	35 (76.1)	25 (78.1)	11 (61.1)	0.534
Asymptomatic [2]	27 (26.7)	11 (22.9)	3 (8.8)	6 (31.6)	0.145
Dyspnea	33 (32.4)	16 (34)	11 (32.4)	10 (55.6)	0.285
Precordialgia typical	37 (36.3)	16 (33.3)	19 (55.9)	7 (36.8)	0.166
Precordialgia atypical	35 (34.3)	20 (41.7)	13 (38.2)	5 (26.3)	0.650
CAD history[3]	5 (4.9)	7 (14.6)	7 (20.6)	1 (5.6)	0.032

CACS = 0 (absent), CACS low (1-100), CACS intermediate (101-400) and CACS high/very high (> 400). [1] values expressed in the form of mean ± standard deviation. Other values expressed in absolute value (n) and relative frequency (%). [2] Some patients have more than one of the symptoms (dyspnea, atypical pain and soreness). [3]Prior history of acute disease

Table 4: Characterization of coronary artery calcium score (CACS) according to the general characteristics, lifestyle, risk factors and symptoms.

Among the risk factors, dyslipidemia showed a higher (70,8%) frequency in the CACS 1–100 group (p=0,01), followed by the CACS 101–400 (68,4%) and CACS>400 (67,6%) groups. The frequency of related symptoms (dyspnea and typical and atypical precordialgia) was not different between the groups. There was no difference in CAD history between the groups (p=0,03), where CACS 1–100 and CACS 101–400 groups showed greater frequencies relative to other groups (Table 4).

The association between the variables of functionality and degree of calcification showed a significant decrease in the distance walked according to severity of CACS (p=0.03); the post test showed differences

between CACS 101–400 and CACS=0 groups (p=0.05). For total FIM, the CACS>400 group presented the lowest average compared with the other groups, with 101.8±13.2 points (maximum=52 points and minimum=119 points) with no significant difference (p=0.397), but indicating a modified functional dependency requiring assistance for 25% of the task.

The Katz index showed lower values in the CACS>400 group, with a minimum of 0 points and a maximum of 6 points, with no significant difference (p=0,224). The Barthel index showed a lower average value in the group with greater severity, i.e., the CACS>400 group, with a minimum value of 25 points and a maximum of 100 points, with no significant difference (p=0,299) (Table 5).

FUNCTIONAL VARIABLES	CACS=0 (N=104)[1]	CACS=1-100 (N=49)[1]	CACS=101-400 (N=34)[1]	CACS>400 (N=19)[1]	P[2]
Distance travelled	392.4 ± 112.6	369.2 ± 105.9	319.6 ± 100.7	326.3 ± 106.9	0.03
Predicted distance (%)	71.6±18.3	69.6±18	59.3±16.9	59.8±18.2	0.02
Self-care	32.2±4.9	32.8±4.6	32.3±3.4	30.5±5.6	0.339
Sphincter control	13.2±1.8	13.4±1.4	13.7±0.8	13.0±1.9	0.315
Transfers	18.7±3.1	19.0±2.9	18.3±2.7	18.2±3.3	0.685
Locomotion	10.3±2.9	10.4±2.5	9.8±2.2	9.0±2.3	0.168
Communication	12.8±2.2	12.9±1.8	13.0±1.5	12.36±2.0	0.635
Cognition	19.2±2.9	19.3±2.5	19.2±2.4	18.7±3.1	0.854
FIM motor	74.5±11.3	75.8±10.1	74.2±6.9	70.8±11.2	0.368
FIM cognitive	32.1±4.6	32.3±4.1	32.2±3.0	31.0±4.5	0.724
FIM total	106.6±14.8	108.2±13.4	106.5±8.7	101.8±13.2	0.397
Katz	4.8±1.5	5.0±1.4	4.5±1.1	4.3±1.2	0.224
Barthel	83.3 ± 15.0	85.3 ± 12.1	82.6 ± 9.3	78.4 ± 13.0	0.299

CACS = 0 (absent), CACS low (1-100), CACS intermediate (101-400) and CACS high/very high (> 400). FIM: functional independence measurement. [1]valu expressed in the form of mean ± standard deviation.[2] Statistical significance value (p < 0.05).

There was a positive correlation between CACS and age (r=0.33, p<0,0001); however, CACS was negatively correlated with locomotion (r= -0,14, p=0.04) in the FIM domain, total FIM (r= -0.166, p=0.017), Katz index (r= -0.21, p=0.002), Barthel index (r= -0.13, p=0.049), and the distance traveled (r= -0.24, p=0.01).

Table 5: Association of variables of functionality according to coronary artery calcium score (CACS)

Univariate analysis showed that the variables associated with functional capacity included age, gender, physical inactivity, dyspnea, and diabetes mellitus, that is, the older the individual was, the greater the chance of functional dependence. Female gender was associated with a greater chance of functional dependence.

Among these factors, sedentariness, dyspnea, diabetes mellitus, and high blood pressure had higher odds ratios, suggesting a greater association with functional dependency.

The CACS groups were not statistically significant, so the CACS>400 group was equal to the other groups (Table 6).

VARIABLES	OR[1]	CI 95%[2]	p[3]
Age	1.015	0.987 – 1.043	0.31
Female	1.407	0.743 – 2.662	0.29
Male	3.000	1.459 – 6.169	0.003
Dyspnea	2.500	1.326 – 4.715	0.005
Diabetes mellitus	2.018	1.056 – 3.856	0.003
Dyslipidemia	1.05	0.563 – 1.961	0.88
High blood pressure	2.143	0.890 – 5.162	0.089
CACS>400	2.443	0.899 – 5.162	0.80
CACS 101-400	1.298	0.561 – 3.000	0.542
CACS 1-100	0.696	0.307 – 1.578	0,386

Logistic regression for method "Backward Wald" as the dependent variable, the functional dependency and independent variables shown in the table. FIM: functional independence measure, CACS: coronary artery calcium score.
OR[1]: odds ratio, 95% [2] CI 95%: confidence interval, [3]Value of significance (p<0.05).

Table 6: Factors associated with functional dependency (FIM)

The final fitted model showed a significant association of functional dependency with sedentary lifestyle (p=0.007) and dyspnea (p=0.008). Regression between angiotomographic data (coronary stenosis and number of arteries) with the distance predicted showed no significant difference.

Patients in the CACS 101–400 group showed a reduction in the average distance walked of 91.0 ± 26.6 m (95% CI 19.9–162.0 and p=0.05). In addition, patients in the CACS > 400 group also presented a reduction in distance traveled of 83.6±31.8 m. It should be noted that patients with dyspnea showed a reduction in distance traveled of 41.7±21.7 m (p=0.044).

4. Discussion

The high prevalence of risk factors for CAD provides evidence of probable interference with functional health. In this study, individuals with higher CACS and higher percentage of stenosis had a higher risk of cardiovascular disease, with a double increase in the probability of functional impairment, in terms of distance walked for the CACS group > 400 and degree of stenosis group > 50%. It is important to evaluate the functionality of these patients to identify the limitations caused by the symptoms of CAD to try to improve functional aspects. The presence of coronary calcification is an important predictor of risk for cardiovascular events. Using CACS, a noninvasive methodology, to assess this enables better cardiovascular risk stratification [15,16,22].

CACS demonstrated a significant association with cardiovascular events during follow-up in the medium and long-term. Our study highlights that CACS measurement is important when associated with risk factors for cardiovascular disease, such as dyslipidemia and diabetes mellitus [17,18].

Previous studies have shown that anthropometric factors such as BMI can contribute to increased functionality in patients with heart disease, particularly heart failure (HF), although we found no differences in HF between the groups analyzed [19,21].

This study showed that the evaluated patients had 28% of functional dependence classified as partially dependent or modified dependence to perform activities of daily living. Therefore, we consider that measures to promote functionality should be carried out in patients with chronic diseases such as CAD, especially regarding physical-functional performance [20,21].

Another important factor that determines functionality is age; the older the patient is, the greater the lack of independence in everyday activities, which contributes to greater morbidity when associated with other risk factors [19,20,21,22,23]. There is a clear association between greater functionality of patients with HF and severity of the disease. Therefore, HF is a predictor of functionality (Katz index) [22,24].

The physical capacity of patients with CAD in this study, assessed using the 6MWT, showed that almost 30% had a functional impact. In an 8-year follow-up study of 600 patients with chronic heart disease, a median 6MWT of 232 m was found, showing that the evolution of the disease leads to an important functional impact [21]. Therefore, when paired with other functional assessment tools, the 6MWT facilitates the assessment of physical and functional capacity and helps guide exercise levels for patients with heart disease. The distance walked can also act as a marker in these patients with chronic heart disease, with distances between 200 and 300 m more predictive of morbidity and mortality [23,29].

Diastolic dysfunction is associated with dyspnea, with greater dysfunction limiting everyday activities of the individual. This was observed in a 5-year study on 395 patients in which diastolic dysfunction correlated with increased mortality [25,26,29,30,31,32]. Patients with CAD may present changes in circulatory and ventilatory power when coronary stenosis and involvement of more than two coronary arteries are present. A study using specific tests and echocardiography observed an increase in ventilatory variables analyzed, with a potential association with the number of arteries affected by stenosis [26,27].

Few studies have examined the exact relationship between CAD and functionality; however, there is clearly a direct relationship between physical ability and functional capacity because of the effect of CAD on cardiovascular, respiratory, metabolic, and muscular systems, confounded by modulation of the autonomic nervous system. This functional impairment results in low exercise capacity [28,29].

Research on subjects with low risk factor profiles predictably showed a lower CACS than those with high risk factors and subclinical atherosclerosis. However, even among individuals with 5–7 risk factors, it is possible to find low CACS, suggesting that measures of risk factor do not fully account for all factors resulting in CAD [30,33,34].

Thus, the CACS is indicated for the assessment of cardiovascular risk, and, when integrated with the functional assessment, it can allow the assessment of the individual's health more broadly. Therefore, the functional assessment in patients with CAD is an important step to explore its impact on autonomy in activities that involve physical effort, especially in periods of change/worsening of the disease.

5. Conclusion

Physical capacity was associated with CACS in the groups with greater severity (> 400 CACS). Sedentary lifestyle and dyspnea were associated with functionality (greater dependence) in patients with higher CACS.

Therefore, a greater functional impact was observed in cases of greater severity of heart disease and, therefore, symptomatic, consequently, with greater limitation in the performance of their daily activities.

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