

## Calcium Score to Evaluate Chest Pain in the Emergency Room

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### Abstract

Some authors have suggested that a zero calcium score (CAC) can be used to rule out the diagnosis of acute coronary syndrome.

Objective this study is to evaluate the diagnostic accuracy of a zero CAC when compared to the coronary computed tomography angiography (CCTA) at the emergency department.

135 symptomatic patients with no previous coronary heart disease (CHD) who presented to the emergency department were submitted to CAC and CCTA to rule out CHD. All patients had normal electrocardiogram and cardiac biomarkers and were TIMI risk score 0 to 2. The CCTA was considered positive if any obstructive lesion (> 50%) was identified.

The mean age was  $51.7 \pm 13.6$  years with 50.6% of men. Seventy-three (54.1%) patients had a calcium score of zero. Of them, 3 (4.1%) had an obstruction > 50% and underwent invasive coronary angiography. Calcium score showed a sensitivity of 92.9%, specificity of 75.3%, positive and negative predictive values of, respectively, 62.9% and 95.9%. Positive and negative likelihood ratios were respectively of 3.7 and 0.09 to detect lesions greater than 50% in the CCTA.

A negative likelihood ratio of 0.09 is very good to rule out most cases of significant coronary obstruction in epidemiologic studies. However, it is important to understand that in a clinical scenario, all evidence including history, clinical examination, data from electrocardiogram and myocardial biomarkers have to be interpreted together. In our study, three cases with a zero CAC score had coronary obstruction higher than 50% at the CCTA.

### Introduction

Acute chest pain is one of the most frequent symptoms in patients presenting to the emergency department (ED). However, the correct diagnosis of acute coronary syndrome (ACS) remains a challenge to physicians and a significant number of patients are incorrectly discharged home, in spite

### Keywords

Calcium/metabolism; Coronary Disease; Chest Pain; Computed Tomography.

of the presence of ACS. Guidelines for the evaluation of acute chest pain suggest the most adequate diagnostic approach in this population is to safely exclude ACS.

The coronary computed tomography (CCTA) has good accuracy for both the exclusion of coronary artery disease (CAD), as well as for the detection of high-grade coronary stenosis<sup>1</sup>. Therefore, it has recently been used for CAD diagnosis, mainly in symptomatic patients with intermediate pretest probability of disease. The ROMICAT trial showed that negative CCTA results for the evaluation of acute chest pain are associated with a good 2-year prognosis, with a cumulative probability of 2-year major adverse cardiac events increased across CCTA strata for CAD (no CAD 0%; non obstructive CAD 4.6%; CAD with obstruction > 50% 30.3%)<sup>2</sup>. Adding CCTA to the current emergency department risk stratification of acute chest pain was more cost-effective when compared to standard care because of reduced recurrence and rehospitalization<sup>3</sup>.

Although CCTA is generally safe and well tolerated, the use of ionizing radiation is a potential drawback of its widespread use. The use of iodine contrast and drugs such as beta-blockers and nitrates may cause hypotension and bradycardia. Other factors, such as increased heart rate, arrhythmias and obesity could affect CCTA image quality and reduce its accuracy. Coronary artery calcium score (CAC), however, is less affected by motion artifacts and by increased heart rate and arrhythmias. It also has the advantage of a lower radiation dose and no need for contrast, beta-blockers or nitrates.

We analyzed the CAC performed to rule out ACS in patients who sought the ED with chest pain using CCTA as the gold-standard. We compared the CAC and CCTA results to evaluate whether the CAC score could be used as sole image modality to screen significant coronary obstruction, defined as obstruction greater than 50% by CCTA.

### Methods

We analyzed 135 consecutive symptomatic patients with no previous history of CAD who sought the ED of a teaching community hospital in São Paulo, Brazil, from February to August 2011. The patients underwent CAC and CCTA scan to rule out significant CAD after normal electrocardiogram, defined as absence of ST depression or elevation, as well as dynamic changes and nonspecific t wave abnormalities; and normal myocardial biomarkers defined as negative troponin and CK-MB at least six hours after the onset of symptoms.

The CCTA was performed with a 64-detector scanner (Phillips Brilliance, Philips Healthcare, Andover, USA) using mainly prospective acquisition, with 120 kV and mA adjusted to body habitus. The CCTA acquisition was performed after

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oral atenolol with a target heart rate of < 65 beats per minute and nitrate 5 mg SL, unless contraindicated. Only 3 patients (4.1%) did not reach the target heart rate and were scanned with retrospective acquisition using dose modulation. The CAC was performed in all patients using prospective acquisition with 120 Kv and mA adjusted to body habitus.

The CAC was calculated using specific software and the results were presented as the Agatston score. The CCTA were read by level III trained physicians using the AHA 17 segment model. The extent of disease was coded as non-obstructive CHD (<50% luminal obstruction) or obstructive CHD (> 50%).

### Statistical analysis

All continuous variables are shown as mean (standard deviation - SD), except for the CAC, which is shown as median and interquartile ranges due to a skewed distribution. All nominal variables are shown as percentages. To compare nominal data among groups the chi-square or Fisher's exact test were used, whereas the T test was used for continuous data. ANOVA, Kruskal-Wallis and chi square were used to compare groups, as appropriate. The significance level of  $p=0.05$  was used. To evaluate the accuracy of the CAC, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated, as well as the positive and negative likelihood ratios, all of them with their respective 95% confidence interval (95% CI).

### Results

We included 135 patients in the analysis (50% female) who had chest pain suggestive of ACS with normal electrocardiogram and myocardial biomarker results and had a TIMI risk score of 0 - 2 points. These patients were submitted to CAC score and CCTA to rule out significant coronary obstruction and the mean radiation dose for CCTA was  $3.5 \pm 1.2$  mSv and  $1 \pm 0.3$  mSv for CAC.

The overall patient characteristics are displayed in Table 1. Among the 135 patients, 73 (54.1%) presented a zero CAC score (45% of men) and 62 (45.9%) had a CAC score > 0.

The patients with CAC = 0 were younger than the patients with CAC > 0 ( $52 \pm 13$  vs.  $65 \pm 10$ , respectively,  $p < 0.0001$ ) and had lower coronary risk factors. The frequency of hypertension (59% vs. 82%,  $p = 0.03$ ), diabetes (14% vs. 19%,  $p = 0.38$ ), and dyslipidemia (19% vs. 34%,  $p = 0.05$ ) was lower in patients with CAC = 0. When we analyzed the 73 patients with CAC = 0, 70 (95.9%) had no significant CHD and 3 (4.1%) had significant CHD (stenosis > 50%). All of them were referred to coronary angiography and underwent coronary angioplasty (Figure 1 and Table 2). The frequency of smoking was 100% in these 3 patients compared to 13% in the other 70 patients ( $p = 0.004$ ) and it was the only difference in risk factors between the two groups.

Table 2 shows the sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios of the calcium score compared to gold-standard with the respective confidence intervals. Results showed a negative likelihood ratio of almost zero and a positive likelihood ratio of 3.8, which is intermediary.

### Discussion

CCTA has been used to rule out ACS in patients with acute chest pain in the ED, especially in those with low to intermediate risk. The absence of coronary stenosis at the CCTA predicts low likelihood for cardiovascular events<sup>4</sup> and it has also shown a significant negative predictive value (99%) for the detection of significant coronary stenosis.

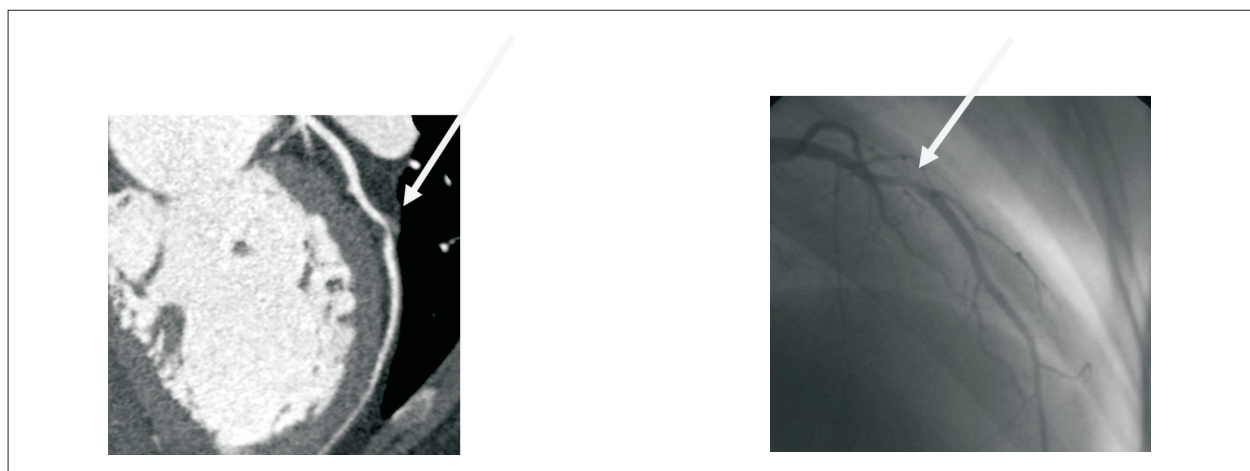
The Multi-Ethnic Study trial (MESA) showed that the asymptomatic patients with no coronary calcium have a low rate of major cardiac events in 5 years; however, these data may not apply to symptomatic patients<sup>5</sup>. A recent study carried out in Korea showed that absence of coronary calcium score could not be used to rule out coronary obstruction > 50% at the CCTA in 15% of Asian patients with acute chest pain<sup>6</sup>. In another cohort study of 279 participants, it was observed that 11.5% of symptomatic patients had > 50% stenosis in one vessel despite zero CAC<sup>7</sup>. These studies suggest that the presence of CAC is not specific for the detection of obstructive CHD and potentially vulnerable lesions, which are commonly seen in ACS and generally non-calcified plaques, being non-detectable by CAC<sup>8</sup>.

**Table 1 – General characteristics of the sample according to presence and severity of stenosis**

Characteristics	No stenosis 69	Stenosis < 50% 24	Stenosis > 50% 42	Total 135	P
Gender (% of men)	32 (46%)	12 (50%)	24 (57%)	68 (50%)	0.54
Age* (years)	$52 \pm 13$	$63 \pm 10$	$65 \pm 11$	$58 \pm 14$	< 0.0001
Hypertension (%)	61%	83%	76%	69%	0.06
Diabetes (%)	11%	16%	24%	16%	0.24
Dyslipidemia (%)	17%	41%	31%	26%	0.04
Smokers (%)	13%	8%	26%	16%	0.10
CAC*	0	45 (23 – 96)	152 (28 – 540)	0 (0 – 75)	< 0.0001

\* the values are mean ( $\pm$  standard deviation). † current use of antihypertensive medicine or systolic blood pressure greater than 140mm Hg. ‡ Total cholesterol > 200 mg/dl or Triglycerides > 150 mg/dl or HDL-Cholesterol < 40 mg/dL for men or < 50 mg/dL for women or use of drugs for dyslipidemia. § Fasting plasma glucose  $\geq 126$ mg/dl or 2-h plasma glucose 200mg/dL or use of drugs for diabetes.

## Brief Communication



**Figure 1** – A. Multiplanar reconstruction of LAD with significant proximal lesion in a patient with normal CAC, confirmed through invasive angiography B. Corresponding invasive angiography image. LAD: left anterior descending artery.

**Table 2** - Sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios of calcium score using the angiotomography of coronary arteries as the gold standard

		Presence of stenosis at angiotomography		
		Yes	No	Total
Calcium score	Positive	39	23	62
	Negative	3	70	73
Total		42	93	135

*Sensitivity of 92.9% (CI: 80.5% - 98.5%), Specificity of 75.3% (CI: 65.2% - 83.6%), Positive predictive value of 62.9% (CI: 49.7% - 74.8%), Negative predictive value of 95.9% (CI: 88.5% - 99.1%), Positive likelihood ratio of 3.7 (2.6 - 5.4), Negative likelihood ratio of 0.09 (0.03 - 0.28).*

CAC is highly sensitive, but less specific for the detection of obstructive CAD, and therefore, excellent for ruling out disease. Consensus statements support the use of zero CAC as a filter before invasive angiography in low-risk symptomatic populations with normal electrocardiogram and myocardial biomarkers; however, when the pretest probability of having obstructive CHD is intermediate, tests with higher specificity (stress testing or CCTA) appear more appropriate as initial tests. Blaha et al. reported situations, using a Bayesian approach, where a zero CAC is helpful and cost-saving, such as for intermediate-risk asymptomatic patients and low-risk symptomatic patients. On the other hand, a zero CAC may not be helpful in very-low risk asymptomatic patients and higher-risk symptomatic patients<sup>9</sup>.

We carried out this report to verify these data in a symptomatic population with no previous CHD who sought a community hospital with possible ACS.

Concordant with previous studies<sup>10</sup>, in our study the zero CAC was not reliable to exclude significant CHD in the minority of symptomatic patients who sought emergency care. Calcification is thought to occur later in atherosclerosis progression and previous studies have suggested that non-calcified plaques are more likely to be present in younger and smoker cohorts of patients.

### Limitations

The number of patients evaluated in this study was small, precluding a more detailed analysis of the cases. We also

considered as gold standard the CCTA results and not an invasive angiography, referring only the patients with significant CHD at the CCTA to invasive angiography.

### Conclusion

A negative likelihood ratio of 0.09 is very good to rule out most cases of important coronary obstruction in epidemiologic studies. However, it is important to understand that in a clinical scenario, all evidence including history, clinical examination, data from the electrocardiogram and enzyme levels have to be interpreted together. In our study, three cases with a zero score had coronary obstruction higher than 50%.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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There were no external funding sources for this study.

### Study Association

This study is not associated with any post-graduation program.

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