

Detection of Coronary Artery Disease Based on the Calcification Index Obtained by Helical Computed Tomography

Carlos Jader Feldman, Domingos Vitola, Nádia Schiavo

Porto Alegre, RS - Brazil

Objective – To assess the relation between coronary artery disease and the calcification index on helical computed tomography.

Method – We studied 22 patients (ages ranging from 40 to 70 years) who underwent coronary angiography because of chest pain suggestive of angina pectoris. Findings on coronary angiography were classified as follows: significant obstructive disease (stenosis $\geq 50\%$), nonobstructive disease (stenosis $< 50\%$), and no disease. With no previous knowledge of the results of the coronary angiography and within 7 days, helical computed tomography of the chest was performed. Then, data of the coronary angiography were correlated with the calcification index obtained by helical computed tomography.

Results – The sensitivity of helical computed tomography to the presence of significant obstructive lesions on coronary angiography was 87.5%, specificity was 100%, and negative and positive predictive values were 75% and 100%, respectively. The mean calcification index was greater in patients with severe coronary lesions, mainly when involvement of 2 or 3 vessels occurred, than that in patients with no coronary artery disease or with nonobstructive coronary artery lesions ($p < 0.05$).

Conclusion – Helical computed tomography is an effective method for detecting and quantifying coronary artery calcification, and it has proved to be sensitive to and specific for the noninvasive diagnosis of coronary artery stenosis.

Keywords – coronary artery disease, coronary arteries, calcification, computed tomography

Coronary artery disease is one of the major causes of morbidity and mortality in industrialized nations. Frequently, acute myocardial infarction or sudden death is the first clinical manifestation of coronary artery disease¹.

Calcification in the intima of coronary arteries results from atherosclerosis and advanced coronary artery disease²⁻⁶. Postmortem studies have shown a correlation between extensive calcification of coronary arteries and the severity of coronary stenoses, as well as the frequency of acute myocardial infarction⁷, even though the occurrence of the latter is strongly related to the lipid content of the atherosclerotic plaque⁸. Segments of arteries with large calcifications had a greater number of atherosclerotic plaques than those segments with fewer calcifications¹. Survival has been shown to be lower in patients with recognized coronary artery disease and calcifications⁹. Other studies^{10,11} have suggested that patients with calcifications in coronary arteries and who undergo thoracotomy have a high incidence of complications.

Early diagnosis and changes in several risk factors are essential elements for reducing mortality or morbidity, or both, in coronary artery disease. However, the early diagnosis and prevention of atherosclerotic coronary artery disease are rendered difficult by the low performance of noninvasive methods for detecting the disease, mainly in young asymptomatic patients¹³. In these patients, early intervention and changes in the risk factors have great value. In many patients with early lesions or still in an asymptomatic phase, stenoses may not be detected¹⁴, showing that calcium detection in coronary arteries is an important predictor of coronary artery disease, mainly in young patients⁹. Therefore, it is important to explore the potential of new techniques for better detecting and quantifying calcifications in coronary arteries¹⁵.

Several imaging techniques, such as fluoroscopy, intravascular echography, conventional computed tomography, electron-beam computed tomography, helical computed tomography, and ultrafast computed tomography are

Instituto de Cardiologia do Rio Grande do Sul - Fundação Universitária de Cardiologia
Mailing address: Carlos Jader Feldman - Unidade de Pesquisa do IC/FUC - Av. Princesa Isabel, 395 - 90620-001 - Porto Alegre, RS, Brazil
English version by Stela Maris C. Gandour

used for detecting calcification in coronary arteries^{2,16,17}. Fluoroscopy has been used for more than 30 years for identifying patients with coronary artery disease^{2,9,18}. Intravascular echography has a greater accuracy for detecting atherosclerosis in an early stage; it is, however, an invasive procedure². Digital fluoroscopy and conventional computed tomography have a greater sensitivity than conventional fluoroscopy for detecting calcifications in coronary arteries. Calcium quantification, however, has not been performed with these methods¹⁵. Computed tomography has a higher sensitivity than fluoroscopy for detecting calcification and allows quantifying calcium deposits. In a study by Agatston et al¹⁵, the sensitivity of ultrafast computed tomography was 96% and that of fluoroscopy was 57%, and this method did not detect moderate calcifications. Another disadvantage of fluoroscopy is dependence on the examiner's observation, who should be a physician, and the results are related to this professional's experience. Ultrafast computed tomography has high-resolution contrast, a rapid image acquisition, and allows elimination of the image blurring due to heart movement^{4,15}, resulting in a high sensitivity for detecting calcium in coronary arteries. Quantifying this calcium may be useful in determining the degree of coronary artery disease. Therefore, and because ultrafast computed tomography is a noninvasive method, it could play an important role in detection of the disease⁴.

In regard to the use of helical computed tomography for this end, data in the literature are scarce, and no study has been carried out in Brazil. This motivated the present study.

Methods

We studied 22 patients, 18 (81.8%) males and 4 (18.2%) females, with ages ranging from 40 and 70 years (mean of 59.6±9 years). They underwent coronary angiography because of chest pain suggestive of angina pectoris. In a blinded study, i.e., without previous knowledge of the results of the coronary angiography, the patients underwent tomographic assessment. The mean time interval between coronary angiography and helical computed tomography was 3.4±2.3 days (ranging from 0 to 7 days), and one patient underwent helical computed tomography one day prior to coronary angiography. Women of childbearing age were excluded from the study.

Helical computed tomography was performed with the use of a helical scanner with a double layer of detectors, and the images were obtained without contrast medium injection. Time of exposure was 1 second for 2 contiguous sections of 2.5mm and ranged from 15 to 22 seconds for the whole region of interest. The test was performed during an unforced maintained inspiration. The effective thickness of the sections was 3.2mm with an increment of 3mm. The total duration of the procedure was 10 minutes.

For calculating the calcification index, 20 more cephalic contiguous sections were selected, the first being at the level of the first visible portion of the trunk or of the anterior

descending artery of the left coronary artery. This allowed a 6-cm coverage of the coronary arteries measured in the longitudinal axis of the patient.

The presence and extension of coronary calcification were determined in each 20 contiguous sections. A calcified lesion was defined as an area inside the coronary artery, whose tomographic density was above 90 Hounsfield units (HU), covering an area $\geq 0.5\text{mm}^2$. The images were revised section by section in a work station, using an automatic program (Escore Cardíaco – Elscint, Israel), in which all pixels were counted with numbers greater than the determined threshold.

The region of interest was demarcated around each lesion (fig. 1) and calculations of the area of the lesion, its tomographic density and score were performed with the program Escore Cardíaco (Elscint, Israel). We obtained scores according to those employed by Shemesh et al² using a minimum threshold of 90 HU. Attenuating factors were determined using the following criteria: factor 1 = 90 – 199 HU; factor 2 = 200 – 299 HU; factor 3 = 300 – 399 HU; factor 4 = ≥ 400 HU. A score for each region of interest was calculated by multiplying the attenuating factor by the area. The total calcification index was determined by adding the scores of the 20 sections.

Coronary angiography was performed according to the technique of Judkins, with multiple oblique projections. Stenoses in the main epicardial coronary arteries were measured with a computed technique and analyzed by two experienced hemodynamics professionals. The coronary angiographic findings were classified as follows: no disease (when no coronary artery lesion existed), significant obstructive disease (when the lesion occupied 50% or more of the arterial diameter of at least one of the major coronary arteries: right coronary artery, anterior descending artery, and circumflex artery), nonobstructive disease (when the stenosis was less than 50%).

Statistical analysis – Sensitivity, specificity, and predictive values were calculated using the 2x2 contingency

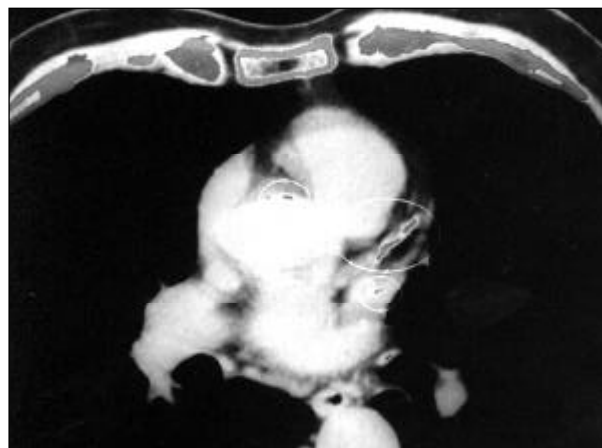


Fig. 1 – Tomographic section showing calcifications in the wall of the ascending aorta and left coronary artery. Note the circles delimiting the lesions for computer reading.

table. To determine the relation between the calcification index and the degree of coronary artery disease, as well as the number of vessels impaired on coronary angiography, we used mean \pm standard deviation of the scores obtained by the program. We used the chi-square test and the *t* test for comparing data. P values <0.05 were considered significant.

Results

The cause of hospital admission was acute myocardial infarction in 41% of the patients and unstable angina in 59%. The presence of one or more risk factors was observed in 86.4% of the patients, 68.2% of them having two or more risk factors, as follows: systemic hypertension (54.5%), smoking (50.0%), dyslipidemia (50.0%), a family history of early atherosclerosis [before 55 years of age (36.4%)], and diabetes mellitus (13.6%). One (4.5%) patient had already undergone myocardial revascularization surgery, and 3 (13.6%) patients had undergone coronary angioplasty. Six (27.3%) patients had a previous history of acute myocardial infarction.

Coronary artery disease was angiographically detected in 18 (82%) patients. Out of these patients, 16 (88.9%) had significant obstructive lesions (stenosis $\geq 50\%$ in at least one of the major coronary arteries), and 2 (11.1%) patients had nonobstructive disease (stenosis $<50\%$). Among the patients with significant obstructive lesions, 8 (50%) had stenosis in 3 vessels, 3 (18.8%) patients had it in 2 vessels, and 5 (31.2%) patients had it in one vessel. The anterior descending artery was impaired in 17 (94.5%) patients, the circumflex artery in 10 (55.5%) patients, and the right coronary artery in 9 (50%) patients. Four (18.2%) patients had normal coronary arteries on coronary angiography.

Coronary artery calcification was found in 14 (63.6%) patients (figs. 2 and 3). Tables I and II show the association between the presence of calcification on helical computed tomography and the presence and degree of coronary artery disease on coronary angiography.

For the possibility of the presence of coronary artery

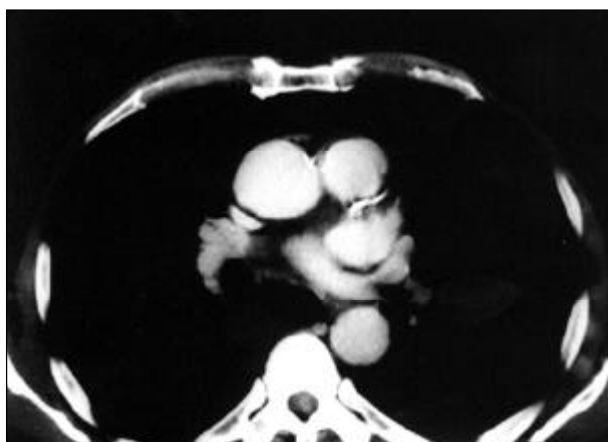


Fig. 2 – Demonstration of calcification in the anterior descending artery in a tomographic section. Calcification is shown as a hyperattenuated area.

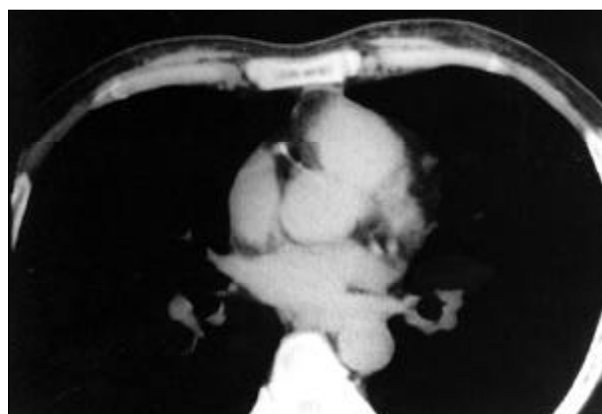


Fig. 3 – Calcification in the right coronary artery shown as an area of greater attenuation in a tomographic section.

Table I – Correlation between the frequency of coronary artery calcification and coronary artery disease

		Coronary artery disease		
		Positive	Negative	Total
Calcification	Positive	14	0	14
	Negative	4	4	8
	Total	18	4	22

Table II – Correlation between the presence of calcification and the degree of coronary artery disease

		Coronary artery disease		
		Absent	Non obstructive	Significantly obstructive
Calcification	Positive	0	0	14
	Negative	4	2	2
	Total	4	2	16

disease on coronary angiography, the sensitivity of helical computed tomography was 78% (14 out of 18 patients), and specificity was 100% (4 out of 4 patients). The negative predictive value was 50%, and the positive predictive value was 100%. Out of the 18 patients with positive findings on coronary angiography, 14 (77.8%) showed calcification on helical computed tomography. In two patients who did not show calcification, atherosclerotic disease was present in one single vessel. In all patients in whom coronary angiography showed nonobstructive disease or absence of coronary lesions, helical computed tomography also detected no calcification. When the population studied was restricted to patients with significant obstructive disease, sensitivity was 87.5% (14 out of 16 patients), and the negative predictive value was 75%. Specificity and positive predictive value remained 100%. Out of the 14 patients with positive findings on helical computed tomography, 13 (92.8%) had calcification in the anterior descending artery, 7 (50%) patients in the circumflex artery, and 2 (14.3%) patients in the right coronary artery. Sensitivity for detecting calcification on helical com-

puted tomography in the anterior descending artery, in the circumflex artery, and in the right coronary artery was 70%, 63%, and 22%, respectively, and specificity was 80%, 100%, and 100%, respectively.

Figure 4 shows the mean of the coronary artery calcification indices on coronary angiography of patients without coronary artery lesions, of patients with nonobstructive disease, and of patients with significant obstructive disease.

Figure 5 shows the mean of the calcification indices in relation to the number of coronary arteries impaired on coronary angiography. When only one coronary artery had a lesion or the coronary arteries were normal, the mean of calcification was 18.5 ± 43.6 , and when 2 or 3 vessels were impaired, the mean of calcification was 78.3 ± 75.7 , the difference being statistically significant ($p < 0.05$).

Discussion

Calcification of coronary arteries has been easily and noninvasively identified and quantified on ultrafast, electron-beam, and helical computed tomography¹⁶. Most of the published studies have shown sensitivity and specificity of ultrafast computed tomography in relation to the presence of coronary artery disease. The sensitivity of the examination ranged from 88 to 100% and specificity ranged from 43 to 100%^{5,6,15}. A review of several studies has suggested that electron-beam computed tomography has a

sensitivity ranging from 80 to 100% and specificity from 47 to 62%¹⁹.

Age and the degree of coronary artery disease influence the values of sensitivity and specificity. Sensitivity increases with the increase in age; specificity, however, decreases¹⁴. The amount of calcium and the number of coronary artery lesions increase with age, but calcification may be independent from the presence or absence of coronary artery disease¹⁵.

Janowitz et al³ analyzed the evolution of the amount of calcium in atherosclerotic plaques obtained by ultrafast computed tomography in patients with and without coronary artery disease. Ninety-eight percent of the calcium deposits identified in a first examination were confirmed on following examinations, and a significant increase was observed in the calcification volume and in the total calcified area of the atherosclerotic plaque in the evolution. Patients with coronary artery disease have a large amount of new calcium deposits, which are not found in asymptomatic patients. In patients with no evidence of calcification, both in the first approach and later, the prevalence of ischemic heart disease is extremely low^{1,5}.

Coronary artery calcification is more prevalent in males than in females, particularly in younger ones. This difference decreases as age increases, being parallel to the clinical manifestations of coronary artery disease. This happens because females are protected against atherosclerosis before menopause due to the female hormones⁴.

In several studies, the relation between the presence of coronary artery disease detected on coronary angiography and the calcification index obtained by computed tomography is high. Prevalence has ranged from 88% to 100%^{2,6,7,14}. Calcifications occur more frequently in the proximal portion of the arteries (around 3cm)². Large amounts of calcium in the plaques are correlated with severe stenoses⁴.

Calcifications found on ultrafast computed tomography usually indicate coronary artery disease, mainly in younger patients in whom calcification of the arteries is not common⁴.

In our study, 14 out of 18 patients with coronary artery disease showed coronary artery calcification on helical computed tomography, comprising a sensitivity of 78%. Specificity and the positive predictive value were 100%, as all patients with no coronary artery disease also had no calcification on helical computed tomography. The negative predictive value was 50% as 4 out of 8 patients in whom no calcification was detected had coronary artery disease on coronary angiography. This happened to lesions in the right coronary artery, where a certain technical difficulty still exists regarding evaluation of the presence of calcium in its topography.

We observed a lower sensitivity (78%) for finding coronary artery calcification on helical computed tomography in patients with coronary artery disease than Shemesh et al² (92%) did. However, our study showed a higher specificity (100% vs 73%). In the group of patients with significant obstructive disease, sensitivity was similar (87.5% vs 91%), but specificity was higher (100% vs 52%).

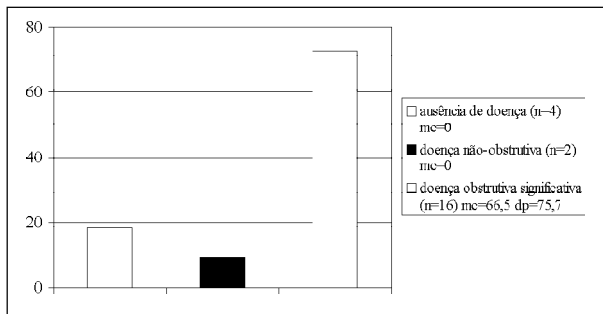


Fig. 4 – Percentage of patients in regard to presence or absence of coronary artery disease and the mean calcification index. n – number of patients; mc – mean calcification; sd – standard deviation

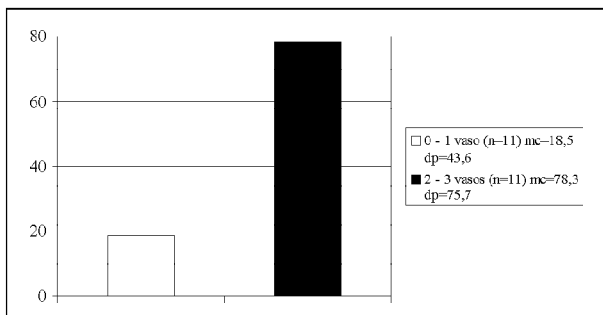


Fig. 5 – Mean calcification index (MC) according to the number of severely impaired coronary arteries. n – number of patients; sd – standard deviation.

In addition to the possibility of detecting the presence or absence of coronary artery disease through a noninvasive method, such as helical computed tomography, analysis of the mean calcification may also differentiate patients with lesions in a single coronary artery from those with disease in 2 or 3 coronary arteries. This is in accordance with a study that employed a methodology similar to ours².

In conclusion, helical computed tomography may be employed as a noninvasive method for detecting coronary artery disease with a high index of sensitivity and specificity. It may also differentiate patients with more severe disease from those with lesions in one single coronary artery, showing, however, in these cases, a high index of false negativity mainly for lesions of the right coronary artery.

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