The prevalence of coronary artery plaques detected by CT angiography in Albanians with no history of cardiovascular disease

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Abstract

Aim: To evaluate the prevalence of coronary artery plaques (CAP) detected by CT angiography in a group of consecutive Albanian individuals with no history of coronary artery disease (CAD) or acute coronary syndrome and investigate the relation between the prevalence of CAP, traditional risk factors and Ca Score.
Methods: This was a prospective study including 456 patients with no history of CAD who underwent CTAC at the American Hospital of Tirana from September 2009 to March 2013. CT scan was performed with a 64 detector CT, including Ca Score and angiography of coronaries with IV contrast.
Results: The prevalence of CAP diagnosed by CTAC was calculated as 55.7%, overall. Significant correlation was found between all traditional risk factors and CAP, except for hyperlipidemia. Though the presence and severity of CAP increased significantly with the increase of Ca Score, 67% of patients of low risk group (Ca score 0-10) had CAP in CT angiography, from these 46.6% were stenotic lesions (>50%) and 5.4% with severe stenosis.
Conclusion: Although a direct relation between the prevalence of CAP, risk factors and the amount of calcium in coronaries was present, a significant prevalence of CAP in low-risk group according to Ca score was found with a considerable presence of stenotic lesions. Although the calcium score does add prognostic value to standard risk factors and serum markers, imaging the vessel wall directly may be helpful to identify CAP and guide therapy.

Keywords: atherosclerosis, calcium, CT angiography of coronaries.

Introduction

The coronary artery disease (CAD) is one of the leading causes of death in Albania with a significant increase in the last decades (1). The conventional coronary angiography is the most used technique, the so called "gold standard" for the CAD diagnosis. Recently, the coronary angiography has been challenged by a new non-invasive technique, the CTAC (CT angiography of coronaries), that has gained popularity in the last decade with the fast development of technology in the field of imaging, increasingly substituting the invasive coronary angiography in CAD diagnosis (2,3). The introduction of multi-slice CT scans with 64 detectors brought a revolution in the imaging of the heart, increasing noticeably the sensitivity and the specificity of this method in the diagnosis of the coronary atherosclerosis up to 99% and 97%, respectively (4). Many recent studies in this field strongly support the usage of CTAC in the diagnosis of CAD as an alternative of the coronary angiography (4-6).

Cardiac risk assessment has been traditionally based on a combination of diabetes, obesity, history of elevated blood pressure, smoking, plasma level of total cholesterol and its fractions and family history of premature coronary heart disease (7,8). Risk factor analysis was introduced to medicine by the Framingham study in 1948 (9). Since then, several risk factor algorithms have been developed with the goal of predicting major or fatal cardio-vascular events (CVE) and to help figuring out the most appropriate individual diagnostic and treatment strategy. However, a significant number of CVEs occur either in the absence of risk factors or in the presence of moderate risk whereby an aggressive treatment strategy would not be indicated (7,10).

In addition, the presence of calcium in the coronary arteries has been shown to be an indicator for atherosclerotic disease (11). The calcium is detectable on CT and is quantifiable using the Agatston method (12,13), which adds prognostic information to available demographic and serologic risk stratification (14,15). However, CT performed for calcium scoring is not able to show noncalcified atheroma or stenosis. Many studies have shown that the Ca score (calcium score) is a diagnostic test with a high negative predictive value of excluding CAD but with low specificity, especially in young ages due to the inability of diagnosing the soft atherosclerotic plaques at high rupture risk (16).

The aim of our study was to: prospectively investigate the prevalence of CAP as detected by CTAC in Albanian individuals with no history of coronary artery disease or acute coronary syndrome in correlation with traditional risk factors and Ca score values.

Material and methods

The group of study

In this study we have included 456 patients without history of CAD that applied for a cardiac check-up or were referred by doctors to the American Hospital of Tirana in order to rule-out coronary atherosclerosis during a period from September 2009 to March 2013. Indications for performing a CTAC were chest pain, shortness of breath, syncope or equivocal stress testing including exercise ECG, myocardial perfusion imaging or stress echocardiography unable to definitively rule-out/rule-in significant coronary artery disease. Exclusion criteria for performing CTAC were renal insufficiency (serum creatinine 120 mol/l), contraindications to the administration of iodinated contrast, pregnancy, acute coronary syndromes and ventricular and/or supraventricular arrhythmias. The research was performed according to the World Medical Declaration of Helsinki principles. All individuals gave informed consent before undergoing the exam.

For each individual, a complete medical history was obtained and a detailed physical examination was performed. Systolic and diastolic blood pressures were measured in the sitting position after five minutes of rest. An individual whose arterial blood pressure was.140/90 mm Hg or was taking antihypertensive medications was classified as having hypertension (17). An individual with a non-fasting plasma glucose concentration of at least 200 mg/dl (11.1 mmol/l), or fasting plasma glucose level of at least 126 mg/dl (7.0 mmol/l), or was being treated with anti-diabetic medication was considered to have diabetes (18). An individual with a body mass index (BMI) (calculated as weight divided by height squared) of 30 kg/m2 or more was considered to be obese (19). A smoker was defined as an individual who smoked at least one cigarette per day or had quit smoking during the previous year. Hypercholesterolaemia was defined as a total serum cholesterol level of 240 mg/dl or more or a serum triglyceride level of 200 mg/dl or more (or both) or use of a lipid-lowering agent (20). Individuals were considered as having a positive family history when they had first-degree or second-degree relatives with premature cardio-vascular disease.

Scan protocol and image reconstruction

Data acquisition was performed with a 64-slice CT scanner (Somatom Sensation, Siemens, Erlangen, Germany), including *Ca Score*- a prospective low dosage examination without contrast agent and after that CT angiography using a retrospective ECG-gating protocol. The bolus tracking technique (SmartPrep) was used to trigger the acquisition, with a four-cavity view as the region of interest. A total of 70–100 ml of iodinated, nonionic contrast agent (Optiray 350, Mallinckrodt) was injected into the antecubital vein at a flow rate of 5.0 ml/s, followed by a 50-ml saline flush injected at a flow rate of 5.0 ml/s. Scanning was initiated during a single breath hold for an acquisition time of 7-10 seconds. 65% of patients required pre-treatment with beta blockers to lower the heart rate. All images were reconstructed with an effective slice thickness of 0.625 mm.

CTAC analysis

Reconstructed image data were transferred to a remote workstation (Leonardo, Siemens) for post-processing. In retrospect, ECG-gating protocol reconstruction of the image data was performed starting from early systole (10% of R–R interval) and ending at end diastole (90% of R–R interval) using 10% steps. Image data sets were reconstructed immediately after the scan and then were analyzed by a specialized radiologist using a dedicated program (Circulation) including MPR, MIP, VRT reconstructions, based on the 16 separate segment model recommended by the American Heart Association (22). CAP was classified into three types: non-calcified, calcified and mixed. Any CAP with a computed tomography attenuation below the contrast-enhanced coronary lumen <130 Hounsfield units (HU), was judged as non-calcified. Any CAP with an attenuation more than 130 HU that could be visualized separately from the contrast coronary lumen was defined as calcified. Any CAP with both the above mentioned tissue characteristics was defined as ‘‘mixed’’ atherosclerotic plaque.

Coronary lumen narrowing was graded semi-quantitatively by visual assessment comparing the luminal diameter of the segment exhibiting the obstruction to the luminal diameter of the most normal appearing site immediately proximal to the plaque. The threshold for the evaluation of stenosis was 50%. The atherosclerotic plaques that caused a stenosis up to 50% of coronary lumen diameter were called nonstenotic, those with a stenosis of >50% were classified as stenotic and were divided in two groups: (a) moderate stenosis for atherosclerotic plaques with a stenosis of 51-70%; and (b) severe stenosis for atherosclerotic plaques causing a stenosis of > 70%. All the patients diagnosed with stenotic CAD according to the above criteria were referred for coronary angiography.

The amount of arterial calcification (Ca score) was also calculated using Agatston method where the coronary calcium was defined as a lesion over 130 HU in a 1 mm2(3 pixel) surface, and according to this result the patients were divided in 4 groups: grade I - Ca score of 0; grade II - Ca score 1-10;

grade III - Ca score 11-100; and grade IV - Ca score 101-400. The risk for having CAD based on Agatston score has been evaluated for the next 10 years (12).

Statistical analysis

Student t test was used to compare data between genders. Logistic regression was also used to evaluate association of the presence of CAP with patients characteristics examined in our study. We also calculated odds ratio (OR) and confidence interval (CI) 95% to measure the strength of the association. P value was calculated for all traditional risk factors.

Results

The median age of our study population was 56,7 years old (range, 48-81 years). About 69% were male and 31% were female. About 61% of the total population had hypertension, 64% had hyperlipidemia, 33% were smokers, 18% were diabetic, 18% were obese, and 17% had positive family history for CAD. Table 1 shows the relationship between the presence of atherosclerotic plaque and the risk factors. All of the risk factors except hyperlipidemia were found to have strong statistical relationship with the development of atherosclerotic plaques.

Table 1. The characteristics of the patients and the correlation between risk factors and coronary atherosclerotic plaque (CAP)

	Patients		Analyses	
Characteristics	**Without CAP (N=202)**	**With CAP (N=254)**	**OR (IC95%)**	**P-value**
Age (years)	52.3	61.1	1.10(1.07-1.13)	<0.001
Sex (M/F)	120/82	194/60	1.91(1.11-3.27)	0.018
Smoking	48	100	4.94 (3.22-7.62)	<0.001
Hypertension	90	164	2.27 (1.53-3.37)	<0.001
Hyperlipidemia	124	166	0.84 (0.56-1.26)	0.433
Diabetes	21	63	2.84 (1.67-4.84)	<0.001
Obesity	28	53	1.64 (0.97-2.81)	0.064
Heredity	19	61	3.04 (1.71-5.60)	<0.001

The prevalence of CAP was calculated as 56%, overall. Though the presence and severity of CAP increased significantly with the increase of Ca Score, 67% of patients of low risk group (Ca score 0-10) had CAP in CT angiography, from these 46.6% were stenotic lesions (>50%) (Table 2 and 3). Also 5.4% of these lesions from the patients of low risk according to Ca score were severe, confirmed also by coronarography (Figure 1 a-c).

Table 2. Comparison of CA score with CT angiography

Ca score	Without CAP (N=202)	With CAP (N=254)	OR (95%CI)*	P-value
				<0.001 (4)†
0	118(25.8%)	49(10.7%)	1.00 (reference)	-
1-10	49(10.7%)	63(13.8%)	1.03 (0.66-1.61)	0.893
11-100	17(3.7%)	59(12.9%)	3.29 (1.82-6.25)	<0.001
101-400	11(2.4)	47(10.3%)	3.94 (1.92-8.33)	<0.001
>400	7(1.5%)	36(7.9%)	4.60 (1.96-12.5)	<0.001

* Odds ratios: with CAP vs. without CAP.

† Overall p-value and degrees of freedom (in parentheses).

Table 3. Comparison of CA score with severity of stenosis

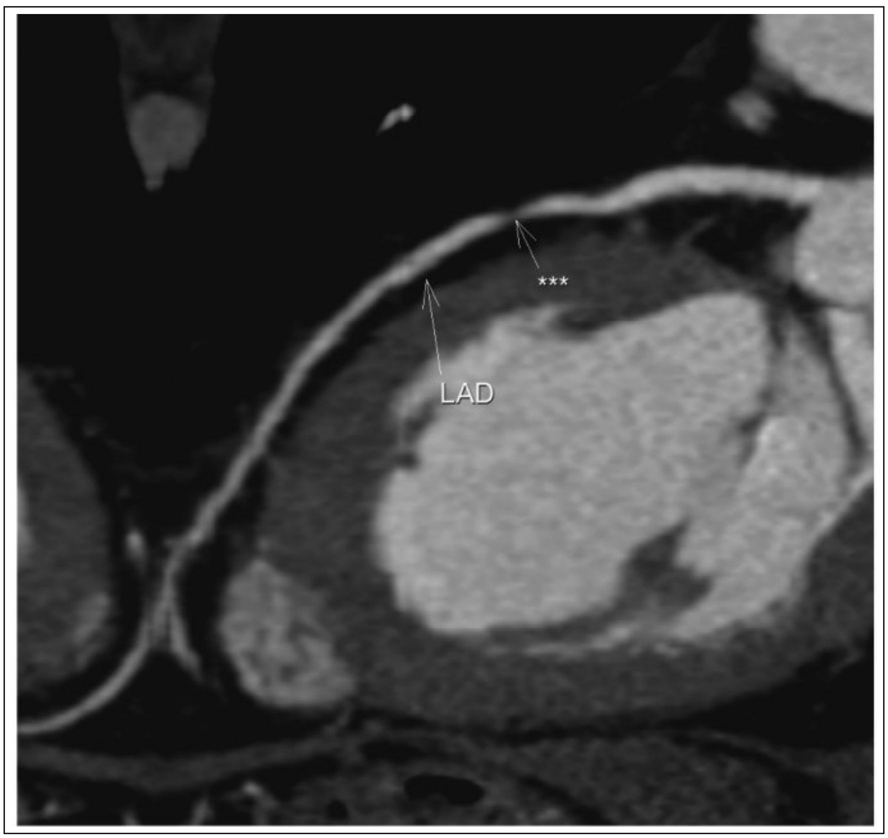
Ca score	Mild	Moderate	Severe	P-value[†]
0	143 (85.6%)[*]	21 (12.6%)	3 (1.8%)	
1-10	76 (67.8%)	32 (28.6%)	4 (3.6%)	
11-100	41 (53.9%)	24 (31.6%)	11 (14.5%)	<0.001
101-400	29 (50%)	12 (20.7%)	17 (29.3%)	
>400	9 (20.9%)	13 (30.2%)	21 (48.9%)	

[*] Row percentages.

[†] P-value from chi-square test.

Figure 1 a-c. A 56-year-old male classified as low risk according to Ca score. A soft concentric stenotic plaque in mid-LAD causing severe subocclusive stenosis (arrows) was diagnosed on CT angiography as shown in the multiplanar (a) and volume rendering images (b). The patient was referred for coronary angiography where the lesion was confirmed (c) and treated with stenting.

Figure 1 a



This demonstrates that CTAC is more sensitive than Ca score in early diagnosis of CAD. In the cases that Ca score is 0-10, this technique is more reliable. In the cases that Ca score has a moderated value, CTAC is more sensitive in predicting the grade and severity of the disease.

Figure 1 b

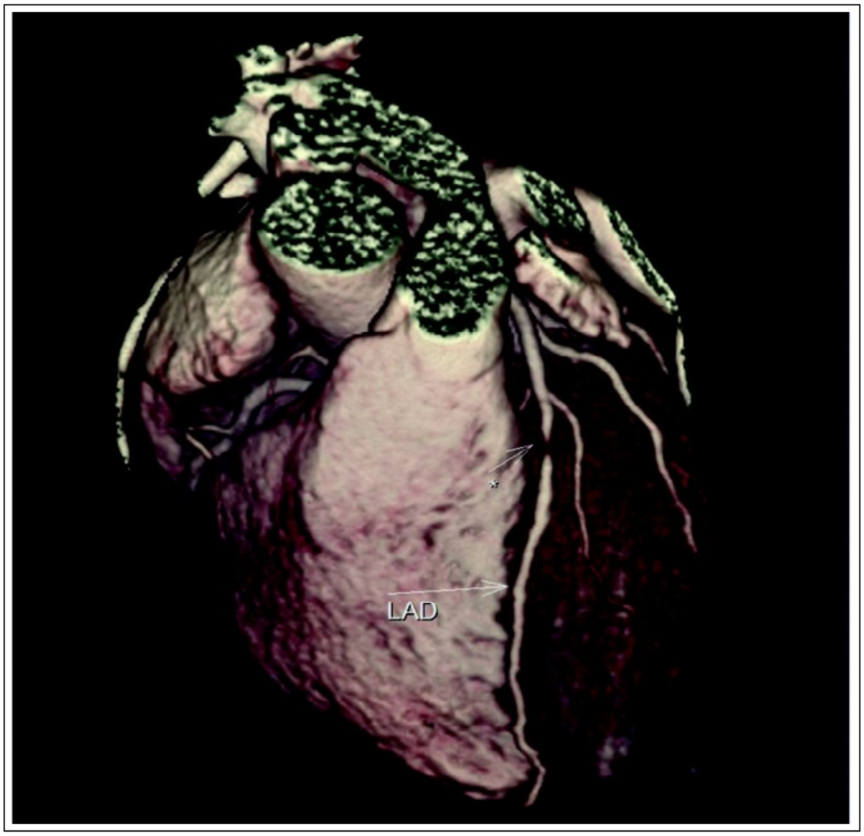
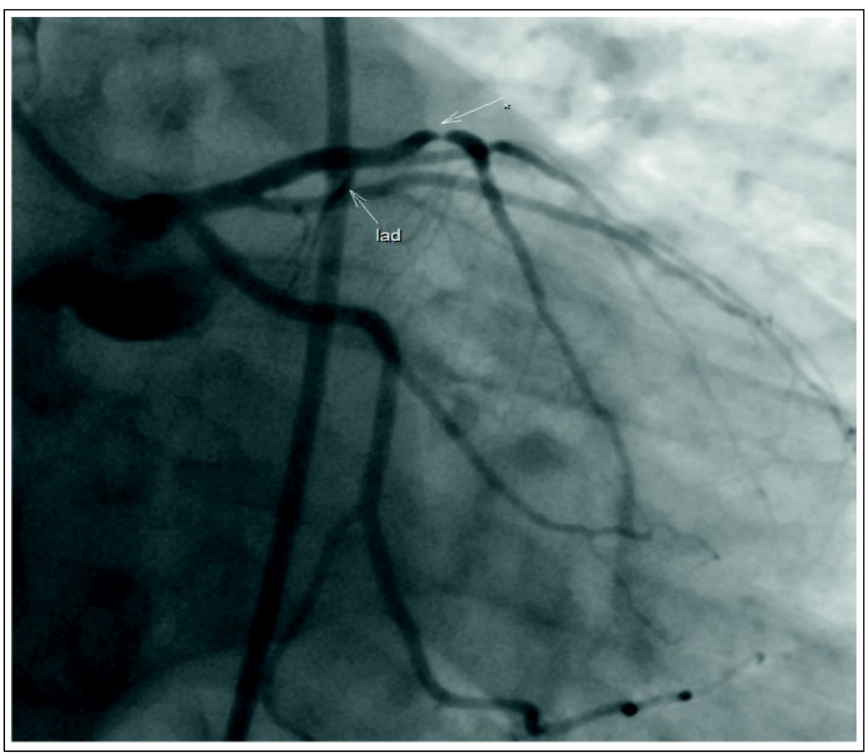


Figure 1 C



Discussion

Computed tomography has emerged as a non-invasive, patient-friendly diagnostic modality to detect the presence of coronary atherosclerosis. The diagnostic potential of computed tomography coronary angiography is high because it allows for not only the detection of significant coronary stenosis but also the presence of non-obstructive coronary plaques (CAP) (4,23). Early subclinical coronary artery disease diagnosed with this non-invasive tool might therefore have a role in refining risk on an individual basis beyond the conventional risk factors or risk estimation algorithms of CVE. There are several recent studies on the association of conventional risk factors with the prevalence and distribution of CAP as detected by CTCA in individuals with no history of coronary artery disease (7,24,25) and to our knowledge, the relation between CAP and risk estimation algorithms remains still unclear.

Even though Albania is classified in the high risk regions of Europe, significant statistical data are lacking in this direction (1,21). Our study population group was classified mainly at low and intermediate risk to develop fatal CVE according to SCORE method. In these individuals, the prevalence of CAP investigated by 64-slice CTAC was 55.7%. Significant correlation was found between all traditional risk factors and CAP, except for hyperlipidemia. Indeed, the lack of statistical significance in the prevalence of hyperlipidemia between the two groups (with CAP vs. without CAP) is appealing. In the absence of any other plausible explanation, we consider this a chance finding.

In our study we found a high prevalence of CAP in the low risk group (0-10) according to Ca Score (67%). This is likely due to the high sensitivity of coronary CTA for plaque detection. Although most of these patients had mild disease, 5.4% showed a significant stenosis and went on coronary stenting.

Calcium scoring has been compared with catheter angiography in several studies, which have reported a very high negative predictive value for significant stenosis (26). Haberl et al. (26) suggested that the absence of coronary calcium is highly predictive of the absence of stenosis, with significant stenosis in <1% of patients with a normal calcium score. Rumberger et al. (27) also found only one significant stenosis on angiography in 65 patients (1.5%) with a normal calcium score. The 5.4% incidence of significant stenosis in our study is higher than those in previous reports.

The true prevalence of subclinical coronary artery disease in the general population is probably unknown, but it is certainly high. Angiographic studies have also documented that acute coronary events are associated with nonstenotic lesions in most cases (28).

Calcium scoring does add useful information for patient risk stratification, as has been shown in multiple studies. However, in our patient population, the clinical utility of a low calcium score was diminished because of the high false-negative rate. Coronary CTA provides significantly more diagnostic information than the calcium score. In patients with a zero calcium score, coronary CTA was able to identify the large percentage of patients with subclinical disease not detected by unenhanced CT. In patients with a positive calcium score, coronary CTA was able to delineate the presence or absence of stenosis with a high degree of accuracy. Essentially, coronary CTA adds certainty to the evaluation of the coronary arteries, whereas the calcium score generates probabilities. Furthermore, 29% of the patients with Ca score zero had CAP in CT angiography and three of them resulted with severe stenotic lesions (Fig.1a-c), supporting the theory that a considerable atheroma burden including significant stenosis may be present in patients with no coronary calcification suggested by previous studies (29).

Our study has several limitations. The main limitation is the radiation exposure. The effective dosage of radiation taken by the patient during this examination varies from 6mSv to 15mSv and that is approximately 1.5-3 times higher than the dosage of invasive coronarography. The new technological developments in this direction promise a considerable reduction of the radiation dosage of up to five mSV through different examination phases (prospective method) (30). The potential advantages of CTAC over other invasive or non-invasive diagnostic procedures for coronary artery disease assessment have to be weighed against the potential hazards associated with long-term radiation risk. Another limitation of our study is that the diagnosis of CAP was based only on CTAC, except cases with moderate-severe stenosis which were confirmed by conventional coronary angiography.

In conclusion, despite its limitations, our study demonstrates once more that CT angiography is a reliable, very accurate non-invasive technique for the diagnosis of early CAD, especially in the low-intermediate risk patients compared to the traditional evaluation schemes and Ca score. Although the calcium score does add prognostic value to standard risk factors and serum markers, imaging the vessel wall directly may be helpful to identify CAP and guide therapy.

Conflict of interest: None declared.

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