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The Role of CT Angiography of Coronaries in Early Diagnosis of Coronary Artery Plaques in Albanian People with No History of Cardiovascular Disease in Correlation with Traditional Risk Factors

Iris Allajbeu, Edjon Hajro, Indrit Temali, Bledi Cekrezi, Krenar Preza

Division of Radiology, American Hospital of Tirana, Albania
Division of Radiology, Mother Tereza University Hospital of Tirana, Albania

Corresponding author: Iris Allajbeu. Division of Radiology, American hospital of Tirana. Albania.

ABSTRACT

Objective: To evaluate the role of CT angiography of coronaries (CTAC) in the diagnosis of subclinical atherosclerosis by detection of coronary artery plaques (CAP) in a group of consecutive albanian individuals with no history of coronary artery disease (CAD) or acute coronary syndrome and to investigate the relation between the prevalence of CAP, traditional risk factors and the expected 10-year risk of fatal cardiovascular event (CVE) based on our own experience. **Method and Technique:** This is a prospective study including 456 patients with no history of CAD who underwent CTAC in our hospital from September 2009 to March 2013. Risk estimation of fatal CVE was assessed using Systematic Coronary Risk Evaluation (SCORE) and then CT scan was performed with a 64 detector CT, including Ca Score and angiography of coronaries with iv contrast. **Results:** From 456 patients 61.4% were low risk and 32.9% were at intermediate risk according to SCORE. The prevalence of CAP diagnosed by CTAC was calculated as 55.7 % overall. Though the presence and severity of CAP increased significantly with the increase of SCORE, it was found to be 44.1% in the low risk patients and 80% in the intermediate risk group, with a presence of 17% and 25% of stenotic plaques (>50%) respectively. Significant correlation was found between all traditional risk factors and CAP. **Conclusion:** Although a direct relation between the prevalence of CAP, risk factors and the related 10-year risk of fatal CVE was found, there was a significant prevalence of CAP in low –intermediate risk group with a considerable presence of stenotic lesions. Also 8.3% of patients with no risk factors and 18% of the patients with Ca score 0 had CAP in CT angiography, one resulting with severe stenosis. Our results suggest once more that CT angiography is a reliable, very accurate noninvasive technique for the diagnosis of early CAD, especially in the low-intermediate risk patients compared to the traditional evaluation schemes and Ca score, thus should be considered in this group as a diagnostic guide for optimal therapy planning .

Key words: CT angiography, coronary plaques, risk factors.

1. INTRODUCTION

The coronary artery disease(CAD) is the main cause of death in many European countries, including Albania (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 noninvasive 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, substituting increasingly 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 obviously the sensitivity and the specificity of this method in the diagnosis of the coronary atherosclerosis up to the values of 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, 5, 6).

Cardiac risk assessment has been traditionally based on a combination of diabetes, obesity, history of elevated blood pressure, cigarette smoking, plasma level of total cholesterol and its fractions, and family history of premature coronary heart disease (1, 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 cardiovascular events (CVE) and to help to find out the most appropriate individual diagnostic and treatment

strategy. However, a significant number of CVE occur either in the absence of risk factors or in presence of moderate risk when an aggressive treatment strategy would not be indicated (1, 10).

Computed tomography has emerged as a noninvasive, patient-friendly diagnostic modality to detect the presence of coronary atherosclerosis. The diagnostic potential of computed tomography coronary angiography is high because it allows not only the detection of significant coronary stenoses but also the presence of non obstructive coronary plaques (CAP) (4, 11). 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 algorithms to estimate risk 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 (1, 12, 13) and, to our knowledge, the relation between CAP and algorithms to estimate risk still remains unclear.

Also the presence of calcium in the coronary arteries has been shown to be a marker for atherosclerotic disease (14). This calcium is detectable on CT and is quantifiable using the Agatston method (15, 16), which adds prognostic information to available demographic and serologic risk stratification (17, 18). However, CT performed for calcium scoring is not able to show non calcified atheroma or stenosis. Many studies have shown that the Ca score (calcium score) is a diagnostic test with a high negative predictive value to exclude CAD but it has a low specificity especially in young ages because of the inability to diagnose the soft atherosclerotic plaques that have a high rupture risk (19).

The aim of our study was to (1) prospectively investigate the prevalence of CAP as detected by CTAC in Albanian individuals with no history of coronary artery disease or acute coronary syndrome; (2) to evaluate the correlation of traditional risk factors with the prevalence of coronary artery plaque and to the expected 10-year risk of fatal CVE.

Also we compared the CTAC and Ca score.

2. METHOD AND TECHNIQUE

The group of study: In this study we have included 456 patients without history of CAD that applied for a cardiac check-up or referred by doctors to our hospital in order to rule-out coronary atherosclerosis 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 performing 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 5 minutes of rest. An individual whose arterial blood pressure was .140/90 mm Hg or was taking antihypertensive medications was classified as having hypertension (20). 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 (21). 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 (22). 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 (23). Individuals were considered as having a positive family history, when they had first-degree or second-degree relatives with premature cardiovascular disease.

The cardiovascular risk was calculated by using the method of SCORE (Cardiology Systematic Coronary Risk Evaluation) as recommended from ESC (European Society of Cardiology). Cardiovascular risk charts based on gender, age, total cholesterol, systolic blood pressure, and smoking status have been developed by ESC for estimating 10-year-risk of a fatal CVE in different European countries (24). Albania is included in the high-risk regions of Europe (24, 25). Based on these risk charts, individuals were classified into high (SCORE > 10%), intermediate to high (SCORE between 4% and 10%) and low (SCORE up to 3%) risk groups.

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, non ionic 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, 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 (26). 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

	Patients		Analyses	
	Without CAP	With CAP		
Characteristics	N=202	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
Arterial 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

Table 1. The characteristics of the patients with and without CAP. CAP, coronary atherosclerotic plaque

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 non stenotic, those with a stenosis of > 50% were classified as stenotic and were divided in two groups: moderate stenosis for atherosclerotic plaques with a stenosis of 51-70% and 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 following 10 years (15).

Statistical analysis: Student t test was used to compare data between genders. Logistic regression was also used to evaluate association of 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.

3. RESULTS

Mean age of our study population was 56,7 years old (range, 48-81 years). 68,9% were male and 31,1% were female. 60,5% of the total population had hypertension, 63,6% had hyperlipidemia and 32,5% were smoker, 18.4% were diabetic, 17.7% were obese, and 17.5% 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.

61.4% of the patients were low risk and 32.9% were at intermediate risk according to SCORE. The prevalence of CAP was calculated as 55.7%. Though the presence and severity of CAP increased significantly with the increase of SCORE, it was found to be 44.1% in the low risk patients and 80% in the intermediate to high risk group, with a prevalence of 17% and 25% of stenotic plaques (>50%) respectively (Table 2, Figure 1, Figure 2, Figure 3). The prevalence dropped to 2% in the low risk group and 7% in the intermediate one when considering severe

Score–group	No. Of cases	%
SCORE 0	38	8.3
CAP(<50%)	4	1.6
SCORE 1-3%	242	53,1
CAP	108	42,5
51-70	16	15
>70	2	2
SCORE 4-10%	150	32,9
CAP	120	80
51-70	22	18,3
>70	8	6,7
SCORE >10%	26	5,7
CAP	22	85
51-70	6	27,3
>70	2	9,1
TOTAL	456	100

Table 2. Summary of the cases with SCORE, CAP positive and Stenosis SCORE, Systematic Coronary Risk Evaluation; CAP, coronary atherosclerotic plaque

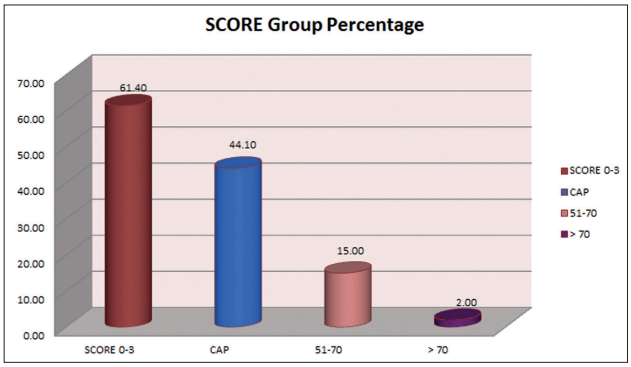

Figure 1. Distribution of cases of low risk , CAP and stenosis according to the SCORE–group.

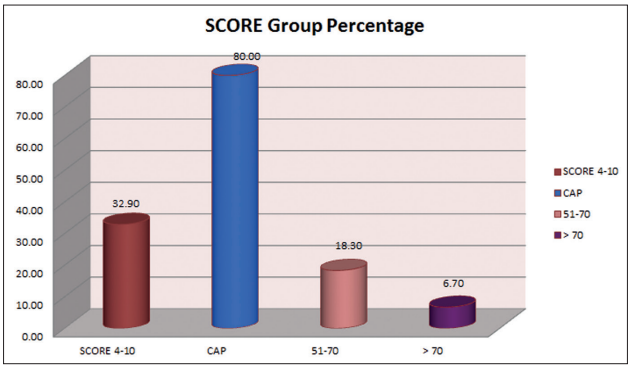

Figure 2. Distribution of cases of intermediate to high risk, CAP and stenosis according to the SCORE–group.

	Patients (%)		Analyses	
Ca score	Without CAP	With CAP	OR (IC 95%)	p value
0	97	18	0,16 (0,11-0,25)	<0,0001
0-11	3	25	1,75 (1,45-2,11)	0,0003
11-100	0	47	2,26 (1,92- 2,66)	<0,0001
100-400	0	18	1,93 (1,69-2,19)	0,0002
>400	1	18	1,82 (1,54-2,15)	0,0008

Table 3. Comparing CT angiography of coronaries with Ca-score. CAP, coronary atherosclerotic plaque; Ca Score, calcium score according to Agatston method

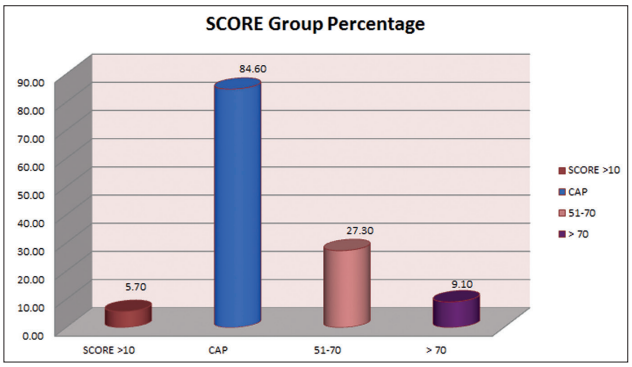

Figure 3. Distribution of cases of high risk, CAP and stenosis according to the SCORE – group

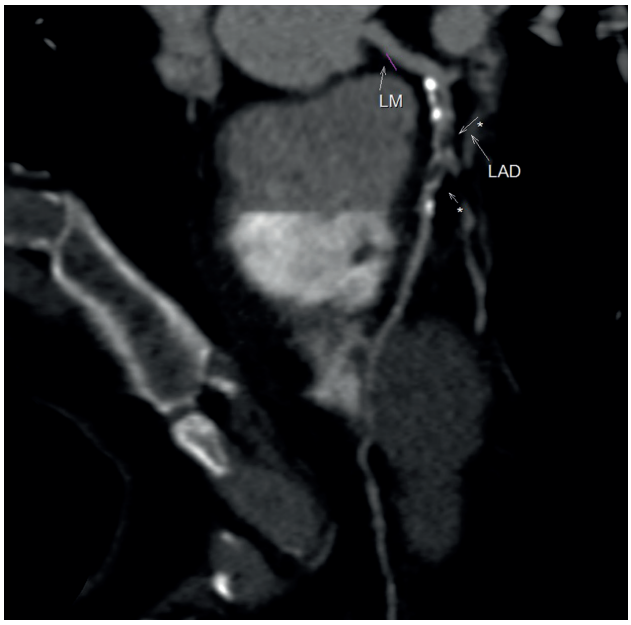

Figure 4. A 46-year-old male classified as low risk according to SCORE. Severe stenotic plaques were found on CT angiography mainly in the proximal LAD. The patient was immediately referred for coronary angiography and underwent stent revascularisation. CT angiography multiplanar reconstruction image showing multiple coronary atherosclerotic plaques on the proximal LAD causing severe stenosis(arrows).

Figure 5. a, b, c. A 56-year-old male classified in intermediate risk group according to SCORE and 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 (Figure 5a) and volume rendering images (Figure 5b). The patient was referred for coronary angiography where the lesion was confirmed (Figure 5c) and treated with stenting.

stenotic lesions (Figure 4 and Figure 5). Furthermore there was no big difference in the presence of CAP between intermediate and high risk group with a slight increase of stenotic lesions in the second one (Figure 3). Also 8.3% of patients with no risk factors (SCORE 0) had CAP in CT angiography (Table 2).

Ca score has also been compared with CTAC (Table 3). 18% of the patients with Ca Score 0 resulted with CAP in CTAC. This demonstrates that CTAC is more sensitive than Ca score in early diagnosis of CAD. In the cases that Ca score is 0, 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.

4. DISCUSSION

To our knowledge this is the first large study performed with CTAC in the Albanian population for ruling out CAD. Even though Albania is classified in the high risk regions of Europe, large statistical data are lacking in this direction (24, 25). 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% . Moreover, our data showed a clear relation between the presence of CAP with an increased predicted risk of fatal CVE . We had a similar prevalence of CAP in the low risk group with a higher presence of stenotic lesions compared to previous studies from the literature(1, 27).Also 8.3% of patients with no risk factors (SCORE 0) resulted with CAP in CTAC. These results support once more the theory that a considerable number of CVE occur either in the absence of known risk factors or in the presence of low to moderate risk (Figure 4, Figure 5) when an aggressive treatment strategy would not be indicated (28).

Also 18% of the patients with Ca score 0 had CAP in CT angiography , one of whom resulted with severe stenotic lesion(Figure 5 a-c), supporting the theory that a considerable atheroma burden including significant stenoses may be present in patients with no coronary calcification suggested by previous studies(19, 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 that is approximately 1.5-3 times higher that the dosage of invasive coronarography. The new technological developments in this direction promise a considerable reduction of the dosage of radiation up to 5 mSV through the 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 weighted 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.

Though we must accept that more tai-

lored analysis should have been done, this is an onging study and we would be glad to share our results modestly.

5. CONCLUSION

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, thus should be considered in this group as a diagnostic guide for optimal therapy planning .

CONFLICT OF INTEREST: NONE DECLARED.

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