Original article

Use of coronary calcium score in the assessment of atherosclerotic lesions in coronary arteries

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Abstract

Introduction: Increased cardiovascular morbidity leads to search for new, non-invasive diagnostic methods for early detection of atherosclerosis. Among others computed tomography has become a matter of interest. The usefulness of quantitative analysis of calcification using multislice spiral computed tomography (MSCT) in cardiology has been studied recently.

Aim: To evaluate the usefulness of calcium score (CS), estimated with MSCT, in identifying the risk of coronary artery stenosis.

Methods: The analysis involved 340 consecutive patients, 222 men and 118 women, mean age 59.7±9.38 years. All patients were admitted to hospital with symptoms of coronary artery disease for coronary angiography. In all subjects risk factor assessment and CS estimation using MSCT were performed.

Results: Mean CS was 271.1±605.9 and it increased with the progression of coronary artery disease. The differences between mean CS values in patients without coronary stenosis and patients with 1-, 2- or 3-vessel disease varied significantly ($p < 0.001$). The cut-off point for total CS for the presence of coronary artery stenosis in the study group was set at ≥56 (sensitivity 85.7% and specificity 85.3%). The likelihood of the absence of significant stenosis (negative predictive value) in the whole study group was 93.5% and in women reached 100%.

Conclusions: Coronary calcium score is a valuable parameter in assessing the likelihood of presence of coronary stenosis. The absence of calcifications in coronary arteries (CS=0) excludes significant coronary stenosis with a high probability.

Key words: coronary calcium score, coronary disease, computed tomography

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Introduction

Epidemiological data indicate that cardiovascular (CV) disease is the leading cause of death in men and women and also the main reason for hospitalisation. Ageing of communities constantly increases the number of patients who need diagnosis and treatment of atherosclerotic diseases, including CV disorders. It inclines investigators to search for new diagnostic methods which identify patients requiring prevention, detailed evaluation or proper treatment. Introduced to clinical practice in the eighties, electron beam computed tomography (EBCT) scanners have become a matter of interest regarding the possibility to image heart structures, due to their good temporal and spatial resolution and thus short acquisition time. In the last few years the technological advances have resulted in considerable improvement of multislice spiral computed tomography (MSCT). Increased number of multidetector rows and slices analysed during one rotation of the detector ring allowed imaging parameters similar to EBCT to be obtained.

Coronary calcium score (CS), a parameter for quantitative assessment of calcifications, was developed based on microscopic observations, which revealed that calcification represents one of the stages of atherosclerotic plaque development. During

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atherogenesis the amount of calcium in plaques increases. The number of calcifications in vessels is an indirect indicator of intensity and duration of atherogenesis [1]. Data from published studies show that MSCT has similar sensitivity for calcification detection as EBCT [2]. In recommendations published in 1996, following critical analysis of available evidence, AHA experts proposed CS assessment as one of the screening tests. According to these guidelines it is recommended to estimate CS in asymptomatic patients with numerous risk factors of atherosclerosis or symptomatic with atypical symptoms [3]. Experts presented propositions of CS interpretation in an ACC/AHA document published in 2000 [4]. The European Society of Cardiology statement on CS values has not been published so far.

The aim of the study was to evaluate the usefulness of CS, estimated with MSCT, in identifying likelihood of coronary artery stenosis.

Methods

Study group

The analysis involved 340 consecutive patients, 222 men and 118 women, aged 59.7±9.38 years (34–81 years) who were referred for MSCT examination and in whom readable tomographic images were obtained. All patients were admitted to hospital with symptoms of coronary artery disease (CAD) for coronary angiography. Patients with previous percutaneous angioplasty or surgical revascularisation, valve replacement, pacemaker implantation, or those with cardiac arrhythmia such as atrial fibrillation or frequent ventricular beats, were excluded from the study. The analysed group of 340 patients constituted 95% of all 359 patients referred for testing.

In 19 patients artefacts hampered a reliable evaluation of scans. Duration of the disease and previous myocardial infarction (MI) were taken into account in past history of the patient. Out of 340 patients of the study group, 144 (42.4%) had MI and the mean duration of CAD was 4.6±4.9 years.

Table I. Characteristics of the study population

	Whole group	Women	Men
Total number	340	118 (34.7%)	222 (65.3%)
Hypertension	242	86 (72.8%)	156 (70.2%)
Hyperlipidaemia	248	81 (68.6%)	167 (75.2%)
Diabetes mellitus	59	21 (17.8%)	38 (17.1%)
Obesity	155	39 (33.0%)	116 (52.2%)
Cigarette smoking	170	28 (23.7%)	142 (63.9%)
Positive family history	109	39 (33.0%)	70 (31.5%)
Previous myocardial infarction	144	35 (27.0%)	109 (49.0%)

In all patients the presence of the following arteriosclerosis risk factors was analysed: age, gender, hypertension, hyperlipidaemia, diabetes mellitus, obesity, positive family history and smoking status. Characteristics of the study group are shown in Table I. Clinical evaluation of the progression of CAD was also performed according to the CCS classification. In the study group, 36 (10.6%) patients were found to be in class I, 182 (53.5%) – in class II whereas 104 (30.6%) and 18 patients (5.3%) were classified in classes III and IV, respectively.

Medical history, physical examination, laboratory tests, computed tomography and coronary angiography were performed in all patients.

Computed tomography

Computed tomography was performed using MSCT – Somatom Plus 4 Volume Zoom machine manufactured by Siemens. Agatston's algorithm was applied to the study group, according to which a lesion was identified as a calcification, if tissue density dependent relative radiation attenuation index, expressed in Hounsfield Units (HU) was 130 or higher. The smallest area of the lesion was 0.5 mm^2. According to the recommended protocols, the thickness of the scanned slice was 3 mm, the time resolution was 125 msec, and the mean scanning time was 16 sec. Images from the diastolic phase of the cardiac cycle, defined using retrospective ECG-gated CT, were taken into analysis. The measurements involved: left main (LM), left anterior descending (LAD), left circumflex (LCX) and right coronary artery (RCA). Calcium score for each single lesion was expressed as a product of the lesion area and so-called index, which varies from 1 to 4, depending on the lesion density. Total coronary CS was determined by summing CS for all coronary arteries. Calcium score is an abstract number and it is counted automatically during image analysis.

Coronary angiography

On angiography, stenosis of ≥50% of the main coronary arteries was considered significant. Time delay between computed tomography and coronary angiography did not exceed three days.

Statistical analysis

Data were analysed using nonparametric tests, due to non-normal distribution of quantitative variables. The distribution was assessed using the Shapiro-Wilk test. Calcium score cut-offs for the presence of significant stenosis were set using receiver operating characteristic curves (ROC), and the specificity, sensitivity and predictive value for estimated cut-off points were assessed simultaneously. Multivariate analysis of the risk model of significant stenosis was undertaken by measurement of the odds ratio (OR) for analysed factors according to the Peto method. Statistical hypotheses were verified at p <0.05 level.

Results

In the group of 340 patients the mean CS value was 271.1±605.9 and varied from 0 to 7001.5. In 92 patients total CS was 0 whereas in 248 subjects its value was above 0.

In 162 (47.6%) patients no significant angiographic lesions were found. In this group, 107 (66%) patients did not have any atherosclerotic lesions in coronary arteries, 17 (10.5%) had lesions reducing lumen area of less than 30%, and 38 (23.5%) patients presented stenotic lesions of 30–40%.

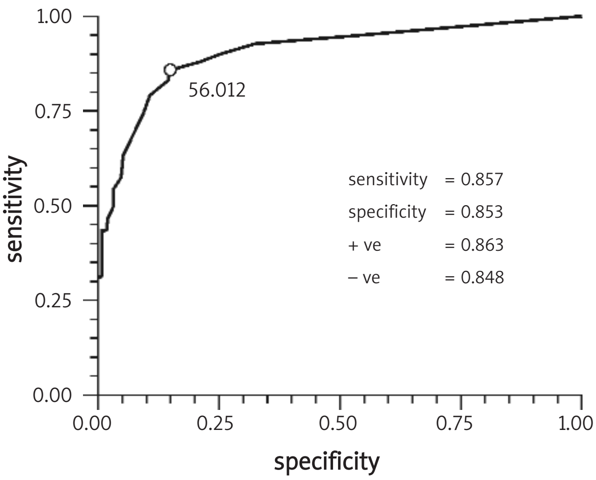
Of 178 patients with significant stenosis, in 67 (37.6%) 1-vessel disease was diagnosed, in 48 (27%) 2-vessel disease, and in 63 (35.4%) – 3-vessel disease. Mean CS value increased along with the severity of CAD, while the differences between mean CS values of patients without coronary stenosis and patients with 1-, 2- or 3-vessel disease, respectively, were significant (p <0.001). The results are shown in Table II.

The ROC curves were computed to assess the usefulness of CS in the assessment of the presence of coronary stenosis, and the cut-off points were established for total CS as well as for the following indices: CS LM, CS LAD, CS CX, and CS RCA. Results are presented in Figure 1 and Table III.

The optimal cut-off point for total CS was set at ≥56 and for LAD, LM, CX and RCA ≥24.8, ≥6.99, ≥4.47 and ≥3.22, respectively. The sensitivity and specificity values of total CS ≥56 were 85.7% and 85.3%, respectively. In 86.3% of patients with CS ≥56, a significant stenosis was observed (positive predictive

Table II. Total CS value distribution depending on CAD severity in angiography. The differences between mean values of CS in groups without significant stenosis and 1-, 2- or 3-vessel disease are significant (p <0.001)

Number of vessels with significant stenosis	Number of patients (n)	CS	
		x ±SD	min-max
0	162	29.4±63.6	0–444.8
1	67	163.4±207.0	0–1025.1
2	48	388.4±309.9	0–1584.0
3	63	917.6±130.3	0–7001.5
Whole group	340	271±605.9	0–7001.5



+ ve positive predictive value, – ve – negative predictive value

Figure 1. The ROC curve showing corresponding sensitivity and specificity values for total CS in predicting coronary artery stenosis

Table III. The analysis of ROC curves for total CS, CS LAD, CS LM, CS RCA and CS CX in order to establish cut-off point for the presence of significant stenosis in particular arteries

Localisation	Cut-off optimal point	Area under ROC curve	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Total CS	56.0	0.907	0.857	0.853	0.863	0.848
LAD	24.8	0.832	0.819	0.697	0.602	0.873
LM	6.99	0.706	0.583	0.838	0.116	0.892
RCA	3.22	0.799	0.807	0.738	0.623	0.876
CX	4.47	0.733	0.615	0.799	0.546	0.841

Table IV. Results of the logistic regression analysis of the effects of analysed factors on the presence of significant coronary stenosis

Factor	Regression coefficient β	OR
Total CS ≥56	2.598	13.435
Obesity	2.161	8.683
Cigarette smoking	0.803	2.232
Positive family history	0.629	1.875
Diabetes mellitus	0.519	1.681
Lipid disorders	0.505	1.658
Age	0.011	1.011

value). The cut-off points established for individual arteries were characterised by low positive predictive value, so they had limited usefulness in estimating the likelihood of presence of stenosis in respective coronary arteries. The sensitivity and specificity values for the prediction of CAD in patients with CS above 0 were also calculated, which means the presence of any calcification in the coronary artery. The values were 96.6% for sensitivity, and 52.4% for specificity.

The next step was to assess the diagnostic value of CS=0 in excluding significant stenosis. Calcifications in coronary arteries were not visualised with the MSCT method (CS=0) in 92 (27%) patients (44 women and 48 men). In no women with CS=0 did angiography show the presence of coronary artery stenosis. In 6 men (6.5% of patients) with CS=0 stenoses of coronary arteries were found on angiography. Single-vessel disease was found in three of them, 2-vessel disease in another 2 men and 3-vessel disease in 1 male patient. The likelihood of the absence of significant stenosis (negative predictive value) in the whole study group was 93.5% and in women reached 100%.

In order to estimate the effects of analysed factors on the presence of significant coronary stenosis, a logistic regression analysis was performed. Presence or absence of significant stenosis was used as the dependent variable y, whereas the following factors were analysed as independent variable x: gender, age, CS ≥56, obesity, hypertension, diabetes, lipid disorders, cigarette smoking and positive family history. The results of logistic regression analysis of the effects of factors on the presence of significant stenosis are shown in Table IV. Total CS had the highest OR, and thus the greatest influence on the presence of significant coronary stenosis in the study group. The classical risk factors such as age, positive family history, diabetes mellitus and lipid disorders were characterised by lower OR. Arterial hypertension did not meet the "entrance" criterion for model OR <1 in the study group.

Discussion

Similarly to us, authors of other published studies have emphasised that the higher the estimated total CS cut-off was identified, the lower sensitivity and higher specificity of stenosis detection were observed [5–8]. In the analysis of a group of 1851 patients referred for coronary angiography due to suspected CAD, Budoff et al. [9] calculated the sensitivity and specificity of CS value >0 to be 95% and 66%, respectively. For cut-off points CS >20, >80, >100 sensitivity was 90%, 79% and 76%, respectively, whereas specificity increased to 58%, 72% and 75%, respectively. Reviewing the literature, significant discrepancies in the values of optimal cut-off points estimated by various investigators for the presence of significant coronary stenosis can be seen. According to the Agatston scale, modified by Mayo Clinic researchers, used for the clinical interpretation of CS, values higher than 400 indicate high probability of significant stenosis [10]. The scale was designed to analyse CS value in screened asymptomatic volunteers whereas we examined symptomatic patients in whom the results of additional tests revealed the presence of CAD, and as many as 144 (42.4%) had prior MI. The variety of measurement techniques as well as the scanners used in investigations, modification of protocols forced by equipment producers and different detection thresholds hinder the comparison of results. Until the recommendations on equipment requirements and standardisation of the study protocol are developed, it will be impossible to assess arbitrary the CS value, which classifies patients to different groups according to the likelihood of coronary stenosis. The age of patients participating in the study is an unquestionable factor determining the critical cut-off point, as well as the presence of risk factors of atherosclerosis and the presence or absence of symptoms.

The present study showed that the localisation of calcifications did not indicate the presence of stenosis in these specific places. The results are consistent with published data [11-13]. In the study performed on 57 patients who underwent EBCT, coronary angiography and ICUS, Baumgart et al. [14] observed that the majority of stenotic lesions in RCA and LAD were calcified, whereas no calcifications within stenotic lesions in CX was observed. This author has shown, like others, that calcifications are observed more often in proximal segments of LAD and CX, and their number decreases distally in these arteries, whereas in RCA calcifications are localised more uniformly, and they are observed in proximal, medial and distal segments [15, 16].

In the present study we aimed to assess the usefulness of the coronary CS in excluding significant coronary artery stenosis. A very high negative predictive value of total CS equal to 0 was found. For the total study population it was estimated at 93.5%, and for female patients – 100%. The results of the present study are consistent with those presented in other papers. Agatston et al. [7] in a study of 584 patients assessed the negative predictive value of CS=0 at 98%. In the study carried out by Haberl et al. [17], calcifications were not found (CS=0) in 14% of the total number of 1764 patients; in this group the likelihood of stenosis was < 1%. In practice this means that a patient with non-specific symptoms and ambiguous results of tests detecting CAD and whose coronary calcium score is equal to 0, has very low probability of significant coronary stenosis. These results confirm the usefulness of CS estimation in screening tests for detection of low risk patients, as well as for establishing indications for coronary angiography in doubtful cases.

To estimate the effects of analysed factors on the presence of significant stenosis a logistic regression analysis was performed. In the study group the highest OR and thus the greatest influence on the risk of significant stenosis had total CS ≥56 (OR – 13.435). Classical atherosclerosis risk factors such as age, positive family history, diabetes mellitus and lipid disorders were characterised by lower OR. Hypertension did not meet the criteria of the entrance model of OR <1 in the analysed group. Schmermund et al. [18] in their study compared diagnostic effectiveness of CS and perfusion scintigraphy as well as risk factor assessment in estimation of CAD progression in 308 patients referred for coronary angiography due to suspected CAD. The patients were divided into two groups: with stenosis of >20% and >50%. Using a multifactor linear regression model the authors demonstrated that total CS was a better independent predictor of the presence of stenosis than SPECT or other risk factors such as age, male gender, or the total cholesterol/HDL index. In the analysis performed by Guerci et al. [13] the highest OR of the stenosis was observed for CS (34.12), and, subsequently, for total cholesterol/HDL index, age, diabetes mellitus and gender. In a study on a Chinese population Chen et al. [19] found very high OR for the presence of coronary stenosis on angiography equal to 120.7 for CS ≥5. Budoff et al. [12] demonstrated that the strongest predictors of stenosis were male gender, CS and the number of vessels with calcifications. According to the Rumberger's theory, calcifications constitute about 20% of atherosclerotic lesion volume, and the atherosclerotic arterial wall forms a mosaic of plaques at different stages of development [20]. That means the more calcifications and non-calcified plaques, and the greater progression of atherosclerosis, the higher likelihood of the presence of stenosis. Calcifications indicate atherosclerotic lesions, whereas the presence of risk factors predisposes to the development of atherosclerotic plaques, but do not prove their presence.

Conclusions

1. Coronary calcium score is a valuable parameter in assessing the likelihood of presence of coronary stenosis. The value of total CS increases together with the number of stenosed coronary arteries.
2. The optimal cut-off value of CS for the presence of significant coronary stenosis was ≥56 in the study population. The sensitivity, specificity and positive predictive values of detection of significant coronary stenosis were: 85.7%, 85.3% and 86.4%, respectively.
3. The localisation of calcifications does not indicate the presence of stenotic lesions in given anatomic locations.
4. The absence of calcifications in coronary arteries (CS=0) excludes significant coronary stenosis with a high rate of confidence.

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Zastosowanie wskaźnika uwapnienia w ocenie zmian miażdżycowych w tętnicach wieńcowych

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Streszczenie

Wstęp: Wzrost zachorowań na choroby układu sercowo-naczyniowego skłania do poszukiwania nowych, nieinwazyjnych metod wczesnego wykrywania zmian miażdżycowych. W kręgu zainteresowań znalazła się także tomografia komputerowa. Ilościowa ocena zwapnień metodą wielorzędowej spiralnej tomografii komputerowej (MSCT) jest obecnie przedmiotem badań w aspekcie przydatności w diagnostyce kardiologicznej.

Cel: Celem badania była ocena przydatności wskaźnika uwapnienia tętnic wieńcowych (CS) oznaczanego przy użyciu MSCT w określaniu prawdopodobieństwa występowania zwężeń w tętnicach wieńcowych.

Metodyka: Badaniami objęto 340 chorych: 222 mężczyzn i 118 kobiet w wieku średnio 59,7±9,38 lat. Chorzy zostali przyjęci do Kliniki z objawami choroby niedokrwiennej serca w celu wykonania koronarografii. U wszystkich pacjentów określono występowanie czynników ryzyka oraz oznaczono CS z zastosowaniem MSCT.

Wyniki: Średnia wartość całkowitego CS wynosiła 271,1±605,9, wzrastała wraz ze wzrostem zaawansowania choroby wieńcowej, przy czym różnice między średnimi wartościami całkowitego CS w grupach pacjentów bez istotnych zwężeń oraz odpowiednio z chorobą 1-, 2-, 3-naczyniową były istotne statystycznie ($p < 0,001$). Wyznaczony punkt krytyczny całkowitego CS dla występowania istotnych zwężeń w tętnicach wieńcowych wynosił ≥56 (czułość 85,7%, swoistość 85,3%). Prawdopodobieństwo braku istotnych zmian w tętnicach (wartość predykcji ujemna) dla CS=0 wynosiło 93,5% w całej badanej grupie, w grupie kobiet 100%.

Wnioski: Wskaźnik CS jest wartościowym parametrem w ocenie prawdopodobieństwa występowania zwężeń w tętnicach wieńcowych. Brak zwapnień w tętnicach wieńcowych (CS=0) z wysokim prawdopodobieństwem wyklucza obecność istotnych zwężeń w tętnicach wieńcowych.

Słowa kluczowe: wskaźnik uwapnienia, choroba wieńcowa, tomografia komputerowa

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