Diagnostic efficacy of coronary calcium score in the assessment of significant coronary artery stenosis

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Abstract

Background: Coronary artery calcium score (CCS) is a quantitative assessment of calcifications detectable by multidetector computed tomography (MDCT).

Aim: To evaluate diagnostic accuracy of CCS to detect significant stenosis in coronary arteries in symptomatic patients.

Methods: The study population included consecutive symptomatic patients with suspected coronary artery disease (CAD) who were referred for coronary angiography. The group included 158 patients (64.6% males) who were all evaluated by unenhanced 64-slice computed tomography where calcium was quantified according to the Agatston method. The ROC curves were constructed to evaluate the discriminating power of the total CCS and CCS for each individual coronary artery in predicting the presence of significant stenosis.

Results: The prevalence of significant CAD strongly increased with higher CCS. The area under the curve (AUC) for total CCS for diagnosing significant stenosis (≥ 50%) in at least one coronary artery was 0.83 (95% CI 0.74-0.92). Using the cut-off value of CCS ≥ 7.7 at least one significant coronary stenosis was detected with the sensitivity and specificity of 86% and 71%, respectively. Significant coronary artery stenosis was better predicted by measuring CCS for individual coronary arteries than total CCS. The AUC of CCS for significant stenosis of each coronary artery was 0.80 for the right coronary artery (RCA), 0.72 for the left main (LM), 0.73 for the left anterior descending (LAD) and 0.76 for the left circumflex arteries (LCX). The optimal cut-off point was estimated for CCS of each coronary artery. It was set at ≥ 3.1 for RCA, ≥ 7.7 for LM, ≥ 9.5 for LAD and ≥ 4.5 for LCX. Positive and negative predictive values for an intact artery using a CCS of zero were 92.8% and 83.8%, respectively. Diagnostic performance of CCS for predicting stenosis of LM and LCX arteries was better in patients over age 65 than in younger patients.

Conclusions: Coronary artery calcium score is useful in predicting coronary artery stenosis, especially in subjects in whom invasive diagnostic or therapeutic utilities seem to be used untimely. The current study suggests an optimal cut-off value of total CCS ≥ 7.7 for detecting significant stenosis, and underlines the better predictive value for CCS of individual arteries.

Key words: coronary calcium score, multidetector computed tomography, coronary stenosis

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Introduction

The needs for diagnostic and screening tools change according to the changing characteristics of the community. Coronary artery disease (CAD) is the leading cause of mortality and morbidity [1] whilst the world population is getting old. Conventional angiography still remains the gold standard for evaluating coronary arteries by revealing location, extent and severity of the stenosis. However, indirect modalities for evaluating coronary arteries have been improved to obtain a better diagnosis, or merely to identify candidates for invasive treatment.

Coronary artery calcium is correlated closely with atherosclerotic plaque formation and thus is a sensitive marker of existing atherosclerosis. It may provide investigators the capability to design new diagnostic methods and may identify patients requiring prevention or proper treatment on time. Coronary artery calcium score (CCS) is a quantitative assessment of calcifications detectable by multidetector computed tomography (MDCT). Studies indicate that it can predict cardiac events in asymptomatic patients [2-4].

Considering the specific abilities of conventional angiography in patients with coronary artery stenosis, non-invasive modalities may effectively guide the treatment strategies to an immediate decision for revascularisation in patients with significant stenosis or to prevent

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unnecessary critical interventions. This study aimed to evaluate diagnostic accuracy of CCS to detect significant stenosis in coronary arteries in a patient-based and vessel-based analysis. This study attempted to integrate the comparison of clinical features with values of CCS (including a zero CCS) and a comprehensive statistical analysis in a large sample of patients.

Methods

Patients

The study population included consecutive symptomatic patients with suspected CAD who were referred for conventional coronary angiography to the University Hospital of Tabriz University of Medical Sciences between September 2008 and September 2009. The study was approved by the Local Ethical Committee of the university and all patients gave written informed consent.

The medical history and risk factors for atherosclerosis were recorded following a physical examination. Previous percutaneous angioplasty or surgical revascularisation, valve replacement, pacemaker implantation and cardiac arrhythmia resulted in exclusion from the study as well as strong evidence for the existence of non-cardiac chest pain. Patients were not included if their serum creatinine level was higher than the normal range, or they were allergic to intravenous contrast materials.

Table I. Characteristics of patients

Parameter	
Age [years]	
whole group	58 ± 10
females	56 ± 9
males	58 ± 10
Male gender, n (%)	102 (65)
Risk factors, n (%)	
hypertension	67 (42)
dyslipidaemia	47 (30)
diabetes	36 (23)
smoking	29 (18)
family history of CAD	16 (10)
Distribution of CAD by conventional angiography, n (%)	
none	36 (23)
one vessel	41 (26)
two vessels	44 (28)
three vessels	37 (24)
Absence of left main coronary artery	6 (4)

Table II. Values of coronary calcium score with respect to the number of coronary arteries with significant stenosis

	Coronary calcium score
Whole study population	198.9 ± 337.5
Patients without coronary artery stenosis	75.4 ± 195.0
Significant stenosis in one artery	88.5 ± 136.5
Significant stenosis in two arteries	168.8 ± 255.7
Significant stenosis in three arteries*	441.1 ± 521.0

** CCS significantly higher than in other groups*

Coronary angiography

The measurements involved the right coronary artery (RCA), left main (LM), left anterior descending (LAD) and left circumflex (LCX) coronary arteries. Stenosis ≥ 50% of the main coronary arteries on conventional angiography (as the reference standard) was considered significant [5]. Conventional angiography was performed by the same independent cardiologist with a digital fluorography system (Siemens Axiom Artis) using a femoral approach. The time delay between computed tomography and coronary angiography did not exceed 24 h.

Multidetector computed tomography

The unenhanced computed tomography was performed at our institution by using a Multidetector scanner (Somatom Sensation 64; Siemens medical solutions, Forchheim, Germany). The finest image quality for all coronary segments was obtained from datasets reconstructed with retrospective ECG gating. The Agatston algorithm was used and total CCS was determined by summing CCS for all coronary arteries. The smallest area of the lesion was 0.5 mm^2. The thickness of the scanned slice was 3 mm, the time resolution was up to 83 msec, and the mean scanning time was 9.25 s.

Statistical analysis

Data were analysed using SPSS software (version 13.0; Chicago). Difference of means was evaluated by ANOVA. Calcium score cut-off values for the presence of significant stenosis were set using receiver operator characteristic curves (ROC) and the related area under the curve (AUC) was provided. Descriptive statistics were used to evaluate the diagnostic performance of CCS to detect significant CAD, including sensitivity, specificity, and positive and negative predictive values for estimated cut-off points. A p-value < 0.05 was considered significant and all comparisons were two-tailed.

Results

One hundred and fifty-eight patients were included in the analysis. Demographic and clinical characteristics are described in Table I. Hypertension was the most frequent CAD risk factor. Mean age of men and women was similar. Stenosis of any degree was observed in 77.7% of patients. This rate was significantly higher in men (84.3%) compared to women (65.5%, $p = 0.007$).

The mean values of CCS in the study group regarding the number of stenotic arteries are presented in Table II. The differences in CCS between patients with stenosis in three arteries and other groups were significant ($p < 0.005$, < 0.005 and 0.001, respectively).

Figures 1 to 4 show the diagnostic performance of CCS for detecting significant stenosis in both vessel-based and patient-based analysis by separate ROC curves. The AUC for total CCS reported by MDCT for diagnosing significant (≥ 50%) stenosis in at least one coronary artery was 0.83 (95% CI 0.74-0.92). The sensitivity and specificity of total CCS for detecting at least one significant stenosis were 86% and 71%, respectively, when using the CCS cut-off value of ≥ 7.7.

On the other hand, a CCS of zero could predict a negative result of conventional angiography in 92.8% of patients (positive predictive value for an intact artery) and could reject detection of stenosis in 83.8% (negative predictive value for an intact artery). The only patient with CCS = 0 and significant stenosis (in LAD) was a 40-year-old male smoker.

We calculated the prevalence of significant stenosis in five ranges of CCS value: 7.1% of patients (1/14) with CCS = 0 had at least one stenotic vessel. This rate was 77.6%, 93.66%, 100% and 87.5% in patients with a CCS of 1 to 100, 101 to 400, 401 to 1000, and > 1000, respectively.

We evaluated the diagnostic accuracy of CCS for detecting significant stenosis. Table III describes the AUC for total CCS for detecting significant stenosis in each coronary artery as well as CCS of the same artery. The optimal cut-off values were estimated for CCS of each coronary artery. It was set at ≥ 3.1 for RCA, ≥ 7.7 for LM, ≥ 9.5 for LAD and ≥ 4.5 for LCX. The sensitivity, specificity, and positive and negative predictive values of the estimated cut-off values for detecting significant stenosis in each artery are described in Table IV.

Diagnostic performance of CCS in LM and LCX arteries was age-dependent and was improved in patients older than 65 years (Table V). Moreover it showed a better diagnostic performance in predicting significant stenosis in RCA and LCX of female patients as well as LM of male patients (Table V).

Discussion

Coronary calcium is closely associated with mural atherosclerotic plaques. Coronary artery calcium assessed by electron beam computed tomography has been extensively evaluated as a diagnostic tool for detecting coronary artery stenosis regarding its non-invasive identification [4] while a similar accuracy has been reported for multi-slice CT scanning [6, 7]. The diagnostic performance of CCS for the degree of stenosis in coronary arteries has been widely considered by recent investigations. Yet there is no consensus and the results vary because of differences in measurement techniques, equipment and protocols as well as analytic approaches. On the other hand, patient classification, diffuse non-significant calcium deposits, remodelling of coronary arteries in response to stenosis and complicated plaques may alter the results.

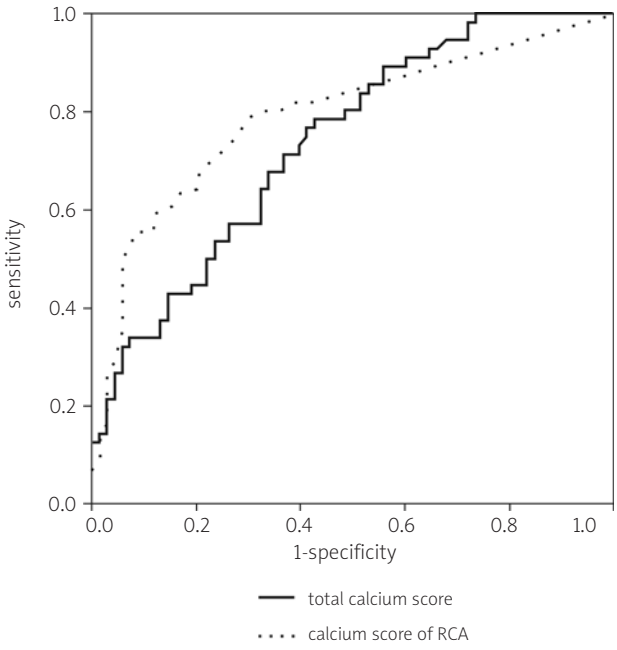

Figure 1. Diagnostic performance of calcium score of right coronary artery (RCA) and total calcium score for stenosis ≥ 50% in RCA

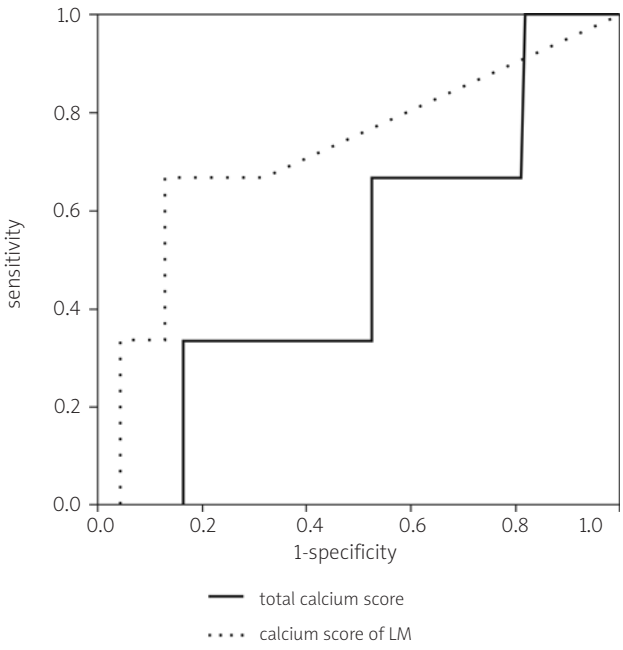

Figure 2. Diagnostic performance of calcium score of left main coronary artery (LM) and total calcium score for stenosis ≥ 50% in LM

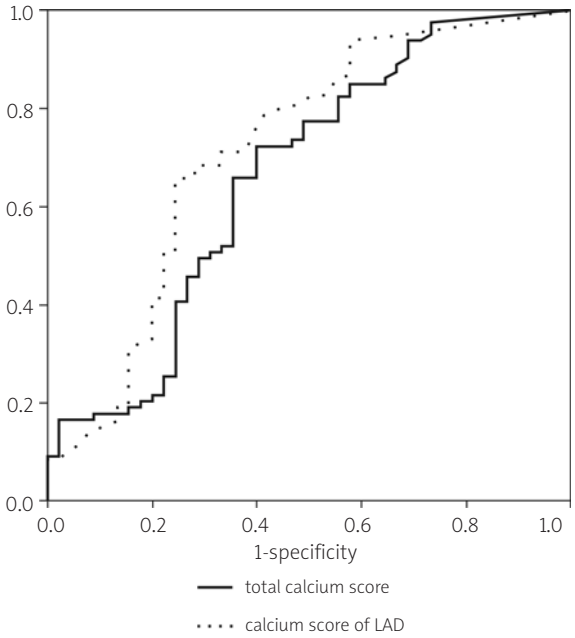

Figure 3. Diagnostic performance of calcium score of left anterior descending coronary artery (LAD) and total calcium score for stenosis ≥ 50% in LAD

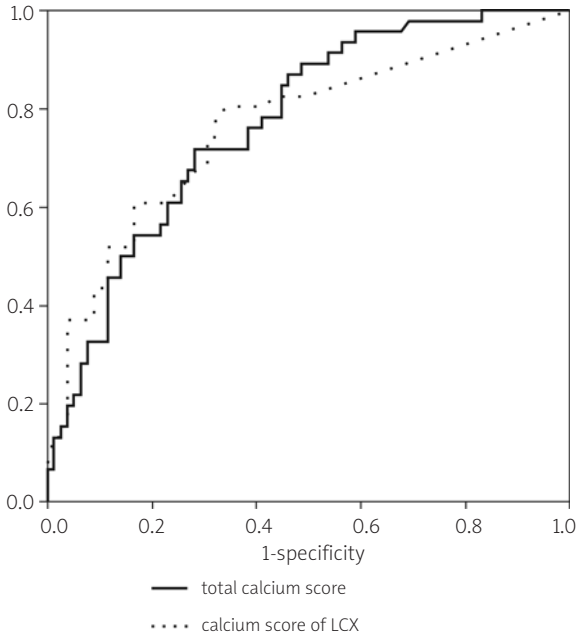

Figure 4. Diagnostic performance of left circumflex artery (LCX) calcium score and total calcium score for stenosis ≥ 50% in LCX

Table III. Area under curve (AVC) and confidence intervals (CI) for diagnostic accuracy of CCS of each coronary artery for diagnosing stenosis in this individual artery

	AUC for CCS of individual artery	95% CI	AUC for total CCS	95% CI
Right coronary artery	0.80	0.71-0.88	0.74	0.65-0.82
Left main coronary artery	0.72	0.38-1.06	0.50	0.20-0.81
Left anterior descending artery	0.73	0.62-0.82	0.66	0.56-0.76
Left circumflex artery	0.76	0.67-0.85	0.78	0.69-0.85

Table IV. Analysis of ROC curves for CCS in each coronary artery to establish optimal cut-off value for diagnosing significant stenosis in that artery

	Optimal cut-off point	Sensitivity [%]	Specificity [%]	Positive predictive value [%]	Negative predictive value [%]
Right coronary artery	3.1	75.0	73.1	68.8	79.4
Left main coronary artery	7.7	66.7	82.2	66.6	82.7
Left anterior descending artery	9.5	70.9	66.7	78.6	58.5
Left circumflex artery	4.5	73.9	69.2	58.6	83.3

The current study was undertaken to determine the performance of quantifying CCS in symptomatic patients in order to establish the CCS cut-off values which may identify patients amenable to the invasive therapeutic approach. This study, like other reports, demonstrated that the 64-slice MDCT scanner provides high-quality non-invasive coronary images that mark out the presence or absence of significant lesions in the main coronary arteries to an acceptable extent. The current study achieved similar results to those reported in a recent study on 664 high risk patients where higher prevalence of stenotic vessels in association with higher scores of coronary calcium was detected [8]. However, there are reports indicating no significant impact of a CCS > 400 on the diagnostic performance of CT angiography in patients referred for conventional angiography [9], compared to the specificity of CCS ≥ 400 to decrease to 20% in another study [10].

Table V. Analysis of ROC curves estimating the area under the curve for calcium score in each coronary artery in different age groups and gender

	AUC for CCS of the artery (CI 95%)			
	Males	Females	≤ 65 years	> 65 years
Right coronary artery	0.74 (0.63-0.85)	**0.87** (0.74-0.99)	0.81 (0.71-0.90)	0.70 (0.48-0.92)
Left main coronary artery	**0.91** (0.81-1.01)	0.35 (-0.11-0.77)	0.63 (0.20-1.05)	**0.95** (0.85-1.0)
Left anterior descending artery	0.670.78 (0.52-0.81)	0.78 (0.65-0.92)	0.50 (0.39-0.62)	0.64 (0.34-0.95)
Left circumflex artery	0.77 (0.65-0.88)	**0.81** (0.67-0.95)	0.75 (0.64-085)	**0.84** (0.66-1.01)
Total CCS	0.76 (0.61-0.92)	0.88 (0.78-0.98)	0.83 (0.74-0.93)	0.82 (0.56-1.07)

A calcium score of zero has been reported by some studies to allow significant stenosis to be ruled out [11], particularly in symptomatic patients [12]. However, we found in our study that despite a high negative predictive value we were not able to definitely exclude significant stenosis in the coronary arteries. This result is in agreement with other recent studies [13]. However, the performance of MDCT imaging of coronary arteries may improve by simultaneous direct imaging of the vessel wall [14]. The better predictive value of individual CCS of each coronary artery, despite insufficient differentiation between the number of affected coronary vessels for total CCS, promises possible improvement of such imaging techniques.

We found lower CCS in our study population compared to studies from other populations from Poland (mean = 271, $p = 0.003$) (15) and the US (mean = 326, $p < 0.005$) [12] which were measured by the same method. Lower carotid intima-media thickness, which is also a reliable indicator of atherosclerosis, in patients with significant coronary stenosis who underwent coronary bypass grafting, was previously reported from our community [16]. Patients involved in the studies evaluating CCS are recruited prior to revascularisation. Thus, one can expect that these patients have a similar stage of CAD. One explanation for the discrepancies between the results of our study and those reported from Poland and the US are differences in patient selection as well as untimely use of invasive diagnostic or therapeutic methods. This emphasises the use of CCS in the assessment process of patients with suspected CAD in our community.

Study limitations

Our study population consisted of selected symptomatic patients who were referred for conventional angiography and accordingly the results only apply to symptomatic patients with strong evidence for cardiac chest pain. Future studies on asymptomatic patients or considering patients with non-cardiac chest pain are needed. We tried to overcome these limitations by increasing the sample size. Moreover, a focus on the diagnostic value of a combination of CCS and CT angiography may be considered in further studies.

Conclusion

The CCS is useful for detecting coronary artery stenosis. This modality is more beneficial in a population where invasive utilities seem to be used untimely. The current study suggests an optimal cut-off value of total CCS ≥ 7.7 for detecting significant stenosis, and underlines the better predictive value for CCS of individual arteries.

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Skuteczność diagnostyczna wskaźnika uwapnienia w ocenie istotnego zwężenia tętnic wieńcowych

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Streszczenie

Wstęp: Wskaźnik uwapnienia tętnic wieńcowych (CCS) jest metodą ilościowej oceny zwapnień wykrywalnych w wielorzędowej tomografii komputerowej (MDCT).

Cel: Ocena trafności diagnostycznej CCS w wykrywaniu istotnego zwężenia tętnic wieńcowych u pacjentów z objawami klinicznymi.

Metody: Badana populacja obejmowała kolejnych pacjentów z objawami klinicznymi, z podejrzeniem choroby wieńcowej (CAD), kierowanych na angiografię. Grupa liczyła 158 pacjentów (64,6% mężczyzn), u których wykonano 64-rzędową tomografię komputerową z ilościową oceną uwapnienia wg metody Agatstona. Wykreślono krzywe ROC w celu oceny mocy dyskryminującej CCS całkowitego oraz CCS dla poszczególnych tętnic wieńcowych pod kątem wykrywania obecności istotnego zwężenia.

Wyniki: Częstość istotnej CAD znacznie wzrastała wraz ze wzrostem CCS. Pole pod krzywą (AUC) dla CCS całkowitego w rozpoznawaniu istotnego zwężenia (≥ 50%) w co najmniej jednej tętnicy wieńcowej wyniosło 0,83 (95% CI 0,74–0,92). Przy użyciu wartości progowej CCS ≥ 7,7 możliwe było wykrycie zwężenia tętnic wieńcowych z czułością i swoistością na poziomie odpowiednio 86% i 71%. Rozpoznawanie istotnego zwężenia przy użyciu CCS dla poszczególnych tętnic wieńcowych było skuteczniejsze niż przy użyciu CCS całkowitego. Pole pod krzywą CCS dla istotnego zwężenia poszczególnych tętnic wynosiło 0,80 dla prawej tętnicy wieńcowej (RCA), 0,72 dla pnia lewej tętnicy wieńcowej (LM), 0,73 dla tętnicy wieńcowej przedniej zstępującej (LAD) i 0,76 dla tętnicy okalającej (LCX). Optymalne wartości progowe określone zostały dla CCS każdej tętnicy wieńcowej: ≥ 3,1 dla RCA, ≥ 7,7 dla LM, ≥ 9,5 dla LAD oraz ≥ 4,5 dla LCX. Pozytywne i negatywne wartości stwierdzenia obecności tętnicy niezmienionej patologicznie przy CCS równym zero wyniosły odpowiednio 92,8% i 83,8%. Skuteczność diagnostyczna CCS w rozpoznawaniu zwężenia LM i LCX była wyższa u pacjentów w wieku powyżej 65 lat.

Wnioski: Wskaźnik uwapnienia tętnic wieńcowych jest użyteczny w rozpoznawaniu zwężenia tętnic wieńcowych, szczególnie u pacjentów, u których diagnostyka lub leczenie inwazyjne mogą być ryzykowne. Niniejsze badanie sugeruje stosowanie optymalnej wartości progowej CCS całkowitego ≥ 7,7 do wykrywania istotnych zwężeń, jak również zwraca uwagę na większą wartość diagnostyczną CCS dla poszczególnych tętnic.

Słowa kluczowe: wskaźnik uwapnienia tętnic wieńcowych, wielorzędowa tomografia komputerowa, zwężenie tętnic wieńcowych

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