ORIGINAL ARTICLE

Effect of coronary artery calcium score on the reduction of global cardiovascular risk

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KEY WORDS ABSTRACT

coronary artery calcium score, prevention, risk factors **INTRODUCTION** There are no studies evaluating an association between different coronary artery calcium scores (CACS) and reduction of traditional cardiovascular risk.

OBJECTIVES The aim of the study was to evaluate the effect of coronary calcium scoring on the reduction of global cardiovascular risk.

PATIENTS AND METHODS This was a prospective single-center study including 180 subjects (mean age, 58.8 years). Calcifications on computed tomography were calculated by 2 experts using the Agatston scale. Selected cardiovascular risk factors and medical procedures used in subjects were analyzed.

RESULTS Invasive coronary angiography was performed in 60 patients (33.2%). It did not show significant coronary lesions in 26 patients (43.3%), while in the other 26 patients (43.3%), coronary angioplasty (stent implantation, balloon angioplasty) was performed. Eight subjects (13.3%) were referred for coronary artery bypass grafting (CABG), and the procedure was performed only in patients with a CACS of 400 AU and higher. Angioplasty was performed 10 times more often in these patients compared with patients with a CACS of 1 to 399 AU. A significant correlation between the CACS and cardiovascular risk was observed in relation to age, weight, and systolic and diastolic blood pressure.

CONCLUSIONS Coronary calcium scoring allows to identify patients requiring invasive coronary angioplasty, or, in some cases, CABG, with greater precision. This can strengthen the role of the CACS as a complement to a classic evaluation of cardiovascular risk factors.

cular deaths. Clinical symptoms usually occur between the age of 50 and 60 years; however, the first symptoms may occur earlier. An increase in the intima-media thickness in 15% of the patients aged from 10 to 20 years has been documented in autopsy research. Symptoms of atherosclerosis have been observed in patients who have suffered from coronary artery disease between the age of 30 and 40 years. The number of calcifications increases in men after 50 years of age and in women after 60 years of age, and this difference is compensated after the age of 70 years.¹⁻³

INTRODUCTION For many years, atheroscle-

rosis has been the leading cause of cardiovas-

One of the first diagnostic methods in atherosclerosis was the measurement of the coronary artery calcium score (CACS) by computed tomography. Coronary calcium scoring is an imaging method using computed tomography to measure the amount of calcium in the coronary arteries. The score is calculated using a weighted value assigned to the highest density of calcification in a given coronary artery (FIGURE 1).

From the beginning, the CACS has been reported to correlate with the risk of coronary stenosis. Rumberg et al.⁴ proved that calcifications had a prognostic value in coronary artery disease (CAD). Similarly, Hoff et al.⁵ noted that the CACS increases along with an increase in traditional risk factors.⁵ Moreover, it correlates with coronary stenosis as observed on invasive coronary angiography. The most recent guidelines from the American College of Cardiology and the European Society of Cardiology have confirmed the usefulness of coronary calcium scoring in asymptomatic patients.^{6.7}

In a meta-analysis, Budoff et al. 8 and Putcher et al. 9 documented that cardiovascular risk

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FIGURE 1 Coronary artery calcium score (CACS) on computed tomography scans; A – CACS reference value; B – CACS = 0 AU; C – CACS = 48 AU; D – CACS = 587 AU



increases along with an increas in CACS as follows: CACS 11–100 Agatston Units (AU) = 2.1-fold; CACS 101–400 AU = 4.1-fold; CACS 401–1000 AU = 6.7-fold; CACS>1000 AU = 10.8-fold. The composite endpoint of myocardial infarction with cardiovascular deaths increased in all groups by 0.4%, 0.7%, 1.6%, 2.2%, respectively.

There is no research evaluating an association between the reduction in traditional cardiovascular risk and various CACS values. The aim of the study was to evaluate the effect of coronary calcium scoring on the reduction of the global cardiovascular risk.

PATIENTS AND METHODS This was a prospective single-center study including 180 subjects (mean age, 58.8 years; women, 50–65 years; men, 40–65 years). Coronary calcium scoring by 64-slice computed tomography was performed in all subjects between 2009 and 2010. Patients were referred for calcium scoring based on the presence of risk factors.

The exclusion criteria were as follows: pregnancy or lactation, claustrophobia, significant heart rhythm disorders, peripheral arterial disease, and chronic kidney disease. Patients with a history of ischemic heart disease, myocardial infarction, coronary artery bypass grafting (CABG), or percutaneous coronary intervention were also excluded.

Patients who entered the study were divided into 3 groups based on CACS results: group 1 with a CACS of 0 AU (n = 56), group 2 with a CACS of 1 to 399 AU (n = 64), and group 3 with a CACS of 400 AU and higher (n = 60). **Coronary artery calcium scoring** Computed tomography was performed using an Aquilion 64 scanner (Toshiba Medical Systems, Japan). Scanning with prospective electrocardiogram-gating was performed during breath-holding using 64 slices with a collimated slice thickness of 3 mm. Breath-holding typically lasted 7 s.

Patients had no special requirements before the procedure, and there was no need to use a contrast agent.

Data were obtained in 2 stages: a pretest to establish the location (FIGURE 2) and coronary calcium scoring (the place of scanning was selected based on the heart rhythm).

The final reconstruction of the data was performed using the Vitrea 2 workstation, versions 3.9.0.0 and 5.1 (Vital Images, United States).

The following scan parameters were used: layer thickness, 3 mm; reconstruction thickness, 3 mm; rotating time, 0.25 s; energy, 120 kV at 300 mA; postprocessing, Toshiba S&S Cardiac Ca Score; postprocessing workstations, Vital Images.

Calcification was calculated using the Agatston scale by 2 experts trained in multislice computed tomography. The coronary arteries were selected manually.

Cardiovascular risk factors The following cardiovascular risk factors were analyzed: arterial hypertension (\geq 140/90 mmHg and/or patients taking hypotensive drugs), hypercholesterolemia (total cholesterol \geq 200 mg% and/or therapy with hypolipidemic drugs), diagnosed diabetes mellitus or therapy with hypoglycemic drugs, overweight

FIGURE 2 Pretest (to identify the location) before coronary calcium scoring; A – posterior--anterior (PA) view; B – posterior-anterior with the area of interest, C – lateral view; D – lateral view with the area of interest



and obesity (body mass index [BMI] ≥25; waist circumference ≥94 cm in men and ≥80 cm in women), abdominal obesity (waist-to-hip ratio [WHR] >0.90 for men and >0.85 for women), past or present smoking, family history (presence of cardiovascular diseases or cardiovascular deaths in parents or siblings under 55 years of age in men and 65 years of age in women), and low physical activity.

Follow-up Clinical data and information about cardiac procedures were collected during a 6-month follow-up. Cardiovascular risk factors were also analyzed.

The study complied with the Declaration of Helsinki and the protocol was approved by the local Ethics Committee (KNW/0022/KB1/133/09).

Statistical analysis All data were analyzed using the Polish version of Statistica 7 (StatSoft, Tulsa, United States). The Shapiro–Wilk test was used to test for normality. Data with normal distribution were analyzed with the *t* test, while data without normal distribution with the Kruskal–Wallis one-way analysis of variance by ranks, a non-parametric method. Distributions were quantified using the χ^2 test.

The Spearman's rank correlation coefficient was used to assess statistical correlations between the CACS and cardiovascular risk factors. Data were log-transformed and presented in the scatter plots. A P value of less than 0.05 was considered statistically significant.

RESULTS The characteristics of the patient groups are presented in TABLE 1. The mean CACS was 0 AU in group 1, 70.7 ±91.5 AU in group 2, and 1107.7 ±1257.9 AU in group 3.

The effective radiation dose during calcium scoring was 0.73 ± 0.33 mSv for all patients (maximum, 2.0 mSv; minimum, 0.45 mSv).

Of 180 patients, 164 (90.6%) were examined by a cardiologist or general practitioner during follow-up. Noninvasive procedures such as an exercise stress test or Holter monitoring were performed in 47 patients (25.9%) after calcium scoring, based on the results.

Invasive coronary angiography was performed in 60 patients (33.2%), of which 26 (43.3%) did not show any significant coronary lesions, while the other 26 patients (43.3%) underwent coronary angioplasty (stents, balloon). Eight subjects (13.3%) were scheduled for cardiac surgery. CABG was performed only in group 3 (CACS \geq 400 AU), while angioplasty was performed 10 times more often in group 3 compared with group 2.

None of the patients with a CACS of 0 AU underwent coronary angiography or angioplasty. Diagnostic and therapeutic procedures performed during a 6-month follow-up are presented in TABLE 2.

The possibility of reducing cardiovascular risk factors was discussed with each patient during the first visit to a general practitioner or a cardiologist. A reduction in the following risk factors was observed 6 months after calcium scoring: BMI in 20% of the patients, WHR in 17%, total TABLE 1 Characteristics of the study groups with different coronary artery calcium scores

		CACS, AU			Duchuc	
		0, n = 56	1–399, n = 64	≥400, n = 60	P value	
sex, n (%)	men	18 (32.1)	24 (37.5)	34 (56.7) 56.7	- 0.017	
	women	38 (57.9)	40 (62.5)	26 (43.3) 43.3		
age, y		54 ±6	59 ±7	62 ±7	0.00001	
place of residence (city), n (%)		50 (89.3)	54 (84.4)	48 (66.6)	NS	
cardiovascular risk fact	ors					
BMI, kg/m ²		27.2 ± 4.5	28.3 ± 5.1	29.3 ± 5.5	0.001	
WHR		0.9 ±0.04	0.9 ± 0.58	0.88 ± 0.09	NS	
abdominal obesity, n (%)		46 (82.1)	50 (78.1)	45 (75)	NS	
systolic BP, mmHg		127.5 ±15.8	131.1 ±13.1	146.6 ±20.4	0.0000	
diastolic BP, mmHg		78.0 ±11.9	77.9 ±10.4	84.4 ±16.9	0.003	
diabetes, n (%)		6 (10.7)	9 (14.1)	19 31.7)	0.004	
smoking, n (%)		9 (16.1)	15 (23.4)	17 (28.3)	NS	
physical activity, n (%)		21 (37.5)	17 (26.6)	25 (41.6)	NS	
hypercholesterolemia, n (%)		31 (55.4)	47 (73.4)	37 (61.6)	NS	
family history of cardiovascular disease, n (%)		41 (73.2)	45 (70.3)	38 63.3)	NS	
marital status, n (%)						
married	married		48 (75)	48 (80)	NC	
single		19 (33.9)	16 (25)	12 (10)	- 113	
education, n (%)						
vocational training		17 (30.4)	22 (34.4)	37 (61.7)	0.001	
general		21 (37.5)	29 (45.3)	18 (30)		
higher		18 (32.1)	13 (20.3)	5 (8.3)		
professional activity, n (%)						
manual work		15 (26.8)	33 (51.6)	26 (43.3)	0.002	
mental work		4 (7.1)	11 (17.2)	15 (25)		
retirement	retirement		18 (28.1)	16 (26.7)	- U.UUZ	
unemployment		5 (8.9)	2 (3.1)	3 (5)		

Data are presented as mean \pm standard deviation or number (percentage).

Abbreviations: BMI – body mass index, BP – blood pressure, CACS – coronary artery calcium score, NS – nonsignificant, WHR – waist-to-hip ratio

TABLE 2 Diagnostic and therapeutic procedures in the study groups during a 6-month follow-up

Variable	Group 1, %	Group 2, %	Group 3, %	<i>P</i> value (χ² test)
follow-up visit	91.1	87.5	95	NS
exercise stress test	5.3	15.6	35	NS
coronarography	0	0.9	50	<0.001
PCA	0	3.1	36.6	NS
CABG	0	0	18.3	<0.001
modification of drug regimen	35.7	37.5%	61.6%	NS

Abbreviation: CABG - coronary artery bypass grafts, PCA - percutaneous coronary angioplasty, others - see TABLE 1

cholesterol in 3.6%, and arterial hypertension in 44.4%. Moreover, smoking cessation was reported in 13.3% of the patients. The highest reduction of risk factors was observed in group 3, although the results for all groups were insignificant. Data on the modification of risk factors according to CACS results are presented in TABLE 3. Significant, but weak, correlations between the CACS and cardiovascular risk were observed in relation to age, weight, and systolic and diastolic blood pressure (FIGURES 3–6). In addition, BMI and CACS tended to be positively correlated (r = 0.1; P = 0.1).

TABLE 3 Modification of risk factors according to coronary artery calcium scores

Dick factor	Group 1		Group 2		Group 3	
	before	after	before	after	before	after
BMI, kg/m ²	27.2 ± 4.5	27.1 ±4.34	28.2 ± 5.1	$27.5~{\pm}6$	29.3 ± 5.5	28.1 ± 4.8
WHR	0.9 ± 0.04	0.89 ± 0.06	0.9 ± 0.58	0.8 ± 0.1	0.88 ± 0.09	0.84 0.09
smoking, %	16.1	12.5	23.4	17.2	28.3	18.3
systolic BP, mmHg	127.5 ±15.8	125.3 ± 12.8	131.1 ±13.1	130.6 ±11	146.5 ± 20.4	138.7 ±14.6
diastolic BP, mmHg	78.0 ±11.9	77.6 ±12.1	77.9 ±10.4	76.3 ± 9.95	84.3 ± 16.9	77.2 ±9.1
hypercholesterolemia, %	55.4	53.1	73.4	71.3	61.6	53.8
physical activity, %	37.5	38.5	26.6	29.7	41.6	42.2

Data are presented as mean \pm standard deviation or number (percentage).

Abbreviations: see TABLE 1

FIGURE 3 Correlation between age and coronary artery calcium score (CACS; logarithmic value) Abbreviations: CI – confidence interval



DISCUSSION Current risk factor evaluation scales such as the Framingham risk score in the United States or SCORE in Europe may not be sufficient to evaluate risk in some patient groups.¹⁰ Coronary calcium scoring may be useful for asymptomatic patients who require extended diagnosis of CAD. Ambrose and Srikanth¹¹ confirmed the usefulness of the CACS for risk evaluation in primary prophylaxis in addition to classic risk calculators and selected biomarkers.

The effect of risk factors on the calcification process has not been fully recognized. Schmermund et al.¹² analyzed this relationship in 211 patients aged from 26 to 79 years. They documented associations between age, sex (male), total cholesterol, high-density lipoproteins (HDL), as well as fibrinogen and coronary calcification and stenosis. Arterial hypertension had a limited effect. Of note, smoking affected the level of CAD but had no effect on calcification.¹² In the present study, we documented that arterial hypertension (both systolic and diastolic), hyperlipidemia, and smoking affect coronary calcium scores and thus the measurement of these factors allows to identify patients at a higher cardiovascular risk.

In a meta-analysis of retrospective and prospective trials conducted to evaluate the role of the CACS, Pletcher et al.⁹ proved that there is a link between calcifications in the coronaries and cardiac events.

In the Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research (EISNER) trial, 2137 patients were randomized into groups with or without coronary calcium scoring. After 4 years of follow-up, changes in selected cardiovascular risk factors were evaluated. Patients who underwent calcium scoring had lower systolic and diastolic blood pressures (P < 0.001), lower total cholesterol (P < 0.001),

FIGURE 4 Correlation between weight and coronary artery calcium score (CACS; logarithmic value) Abbreviations: see FIGURE 3

FIGURE 5 Correlation

between systolic blood pressure and coronary

artery calcium score

(CACS; logarithmic

Abbreviations: see

value)

FIGURE 3



low-density lipoprotein (P < 0.001), and triglycerides (P < 0.001), a greater reduction in weight (P < 0.001), and lower Framingham cardiovascular risk (P = 0.003). Our conclusions are similar to those drawn from the EISNER study because we also observed a reduction in selected cardiovascular risk factors after 6 months of follow-up. Of note, the results of the 2 studies are strengthened by the fact that the studies were performed on different populations with different lifestyles.¹³

Elias-Smale et al.¹⁴ examined 2028 patients with Framingham cardiovascular risk who were reclassified into the high-, average-, and low-risk groups by using CACS results during 10 years of follow-up. Of all patients, 52% were reclassified into groups with lower or higher cardiovascular risk. The CACS was described as an important additional tool to classic risk factors.

Haberl et al.¹⁵ proved that patients with no coronary calcifications (CACS = 0 AU) in the range FIGURE 6 Correlation between diastolic blood pressure and coronary artery calcium score (CACS; logarithmic value) Abbreviations: see FIGURE 3



of 96% to 100% could avoid classic invasive coronary angiography.

Coronary calcium scoring in asymptomatic patients with a moderate risk of CAD may help in diagnostic and therapeutic decisions. It may also facilitate the selection of patients who will benefit from extended diagnostic procedures. The results of a meta-analysis of randomized clinical trials confirmed the usefulness of CACS in asymptomatic subjects.^{16,17}

The Muscatine Study,¹⁸ which investigated risk factors in young adults, reported associations between the BMI, arterial hypertension, elevated triglyceride levels, and low HDL levels and coronary calcification.

Our results confirmed that coronary calcium scoring is a useful examination in asymptomatic patients. Appropriate use of the CACS results can facilitate further diagnostic and therapeutic decisions. Additionally, the examination itself can stimulate patients to change their lifestyles and thus reduce risk factors in most cases. Owing to its simplicity, the procedure may also be used by medical professionals who are interested in prevention as an important factor in the reduction of cardiovascular diseases in Europe. Importantly, our study is the only such study conducted in Europe because they are less common here than in North America.

Our study has several limitations including a relatively small group of patients and short follow-up. Nonetheless, most of our results reached statistical significance.

In conclusion, CACS results allow to identify patients requiring invasive coronary angioplasty, or in some cases, those requiring CABG. This may strengthen the role of coronary calcium scoring as a complement to classic cardiovascular risk assessment.

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ARTYKUŁ ORYGINALNY

Wpływ pomiaru wskaźnika uwapnienia tętnic wieńcowych na obniżenie globalnego ryzyka sercowo-naczyniowego

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SŁOWA KLUCZOWE STRESZCZENIE

czynniki ryzyka, prewencja, wskaźnik uwapnienia tętnic wieńcowych

WPROWADZENIE Brakuje badań naukowych oceniających związek między redukcją tradycyjnych czynników ryzyka a wskaźnikiem uwapnienia tętnic wieńcowych (*coronary artery calcium score* – CACS). **CELE** Celem pracy była ocena wpływu badania CACS na obniżenie globalnego ryzyka sercowo-naczyniowego.

PACJENCI I METODY Badanie zaprojektowano jako prospektywne badanie jednoośrodkowe, do którego włączono 180 pacjentów (średni wiek 58,8 lat). Uwapnienia w tomografii komputerowej zostały wyliczane przez 2 ekspertów za pomocą skali Agatstona przy użyciu półautomatycznych ustawień "2DVScore with Color". Analizowano wybrane czynniki ryzyka sercowo-naczyniowego wraz z procedurami medycznymi, którym poddani byli pacjenci.

WYNIKI Inwazyjną koronarografię wykonano u 60 pacjentów (33,2%). Spośród nich badanie inwazyjne nie wykazało znaczących zmian w naczyniach wieńcowych u 26 pacjentów (43,3%), podczas gdy u kolejnych 26 (43,3%) wykonano angioplastykę wieńcową (implantację stentu, plastykę balonową). Pomostowanie aortalno-wieńcowe (*coronary artery bypass grafting* – CABG) wykonano u 8 chorych (13.3%) – procedura ta była wykonana wyłącznie u pacjentów z CACS ≥400 AU. Angioplastykę wykonywano 10 razy częściej w tej grupie pacjentów w porównaniu z grupą z CACS 1–399 AU. Zaobserwowano istotne korelacje między CACS i ryzykiem sercowo-naczyniowym w zależności od wieku, wagi oraz skurczowego i rozkurczowego ciśnienia tętniczego.

WNIOSKI CACS umożliwia dokładniejszą kwalifikację do zabiegów angioplastyki wieńcowej czy w niektórych przypadkach CABG. Może to wzmacniać rolę CACS jako znaczącego dodatku do analizy czynników ryzyka sercowo-naczyniowego.

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