Research Article / Araştırma Makalesi

Factors Affecting The Change in Agatson Score in Follow Up Multislice Coronary Ct Angiograms

Çok Kesitli Koroner Bt Anjiyografilerde Takipte Agatston Skorunun Değişimine Etki Eden Faktörler

Mustafa Aytek ŞİMŞEK [1], Ayça TÜRER CABBAR [1], Olcay ÖZVEREN [1], Çiğdem KOCA [1], Erdal DURMUŞ [1], Muzaffer DEĞERTEKİN [1],

[1] Yeditepe University School of Medicine Cardiology Department, İstanbul, TURKEY

Background: Coronary calcium shows the atherosclerosis burden in coronary arteries and is associated with adverse cardiac events. Agatston score is the most widely used scoring system to quantify coronary artery calcium. In this study, we aimed to establish the factors associated with the change in Agatston score in time.
Materials and Methods: Patients who underwent multiple coronary computerized tomographic angiographies and had Agatston score measurements were included in the study. The change of Agatston score was compared among cardiovascular risk groups. Linear regression model was formed to detect independent variables affecting the change in Agatston score.
Results: A total of 126 patients were included in the study. 63 patients had zero baseline Agatston score. Patients with hypertension, diabetes or previous coronary artery disease history had significantly higher Agatston score changes than those without. Age and previous coronary artery disease increased the risk of Agatston score increase over time whereas zero baseline Agatston score decreased the risk.
Conclusions: Age and previous coronary artery disease history are independent risk factors for the increase in Agatston score over time. Baseline Agatston score of zero decreases the risk of subsequent increase in Agatston score.

Key Words: Agatston score, Coronary artery calcium, Cardiovascular risk factor

ÖZ.

Amaç: Koroner kalsiyum skoru koroner arterlerdeki ateroskleroz yükünü gösterir ve olumsuz kardiyak olaylar ile ilişkilidir. Agatston skoru koroner arterlerdeki kalsifikasyonun sayısal değerlendirmesi için en sık kullanılan skorlama sistemidir. Bu çalışmada zaman içerisinde Agatston skorundaki değişime etki eden faktörleri saptamayı amaçladık.
Materyal ve Metod: Zaman içerisinde birden fazla koroner bilgisayarlı anjiyografi çekimi yapılmış ve Agatston skoru hesaplanmış hastalar çalışmaya alındı. Agatston skorundaki değişim farklı kardiyovasküler risk grupları içerisinde karşılaştırıldı. Agatston skorundaki değişime etki eden değişkenleri saptamak için doğrusal regresyon modeli oluşturuldu.
Bulgular: 126 hasta çalışmaya dahil edildi. 63 hastanın bazal Agatston skoru sıfırdı. Hipertansiyon, diyabet veya daha önce koroner arter hastalığı öyküsü olan hastalarda olmayanlara göre Agatston skorundaki değişim anlamlı olarak daha fazlaydı. Yaş ve daha önce koroner arter hastalığı öyküsü olması zaman içerisinde Agatston skorunda artış riskini arttırırken, bazal Agatston skorunun sıfır olması bu riski azaltmaktaydı.
Sonuç: Yaş ve daha önce koroner arter hastalığı öyküsü olması Agatston skorunda zaman içerisinde artış için bağımsız risk faktörleridir. Bazal Agatston skorunun sıfır olması ise takipte Agatston skorunun artış riskini azaltmaktadır.

Anahtar kelimeler: Agatston skoru, Koroner arter kalsiyumu, Kardiyovasküler risk faktörü

Corresponding Author / Sorumlu Yazar

Dr. Mustafa Aytek ŞİMŞEK
Yeditepe Üniversitesi Hastanesi,

Yeditepe University Hospital
Icerenkoy District Hastahane Street no:4
Atasehir-Istanbul Turkey

E-mail: m.simsek@gmail.com

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Introduction

The presence of coronary calcium is a marker of coronary atherosclerosis (1). The amount of coronary calcium shows the magnitude of coronary atherosclerosis burden. Coronary artery calcium (CAC) is also associated with adverse cardiovascular outcomes (2). There are several imaging techniques to establish CAC. The most widely used non-invasive method is computed tomography (CT) due to its rapidity, availability, and high sensitivity to detect calcium. Agatston score which is developed by Agatston et.al, uses the amount and maximal CT attenuation of the calcified lesions in coronary arteries to generate a score (3). Age and gender should be taken into consideration when interpreting the score. Current guidelines recommend using CAC evaluation to further adjust the preventive measures in asymptomatic patients with intermediate cardiovascular risk (4).

In this study we aimed to determine factors related with the change in Agatston score in time in patients who had coronary CT imaging more than once.

Materials and Methods

Selection of the participants

Consecutive patients between January 2009 and December 2014 in a single center who had multiple coronary CT imagings and Agatston score calculations at least 12 months apart during follow up were included in the study. Demographical and clinical parameters were obtained from patient files and hospital recordings. Patients who had history of coronary bypass surgery, coronary artery stenting and chronic renal disease (glomerular filtration rate below 60 ml/min) were excluded. The study protocol was approved by local ethical committee (Yeditepe University Non-interventional Clinical Trials Ethics Committee 21/06/2021 -29).

Calculation of Agatston score

Multislice coronary CT angiographies were performed with 128 slice Philips Brilliance CT scanner. (Philips Healthcare, Netherlands). Agatson scores were calculated automatically by integrated software. All images were obtained electrocardiography (ECG) gated.

The baseline Agatston score was defined as the first Agatston score that was recorded and the final Agatston score was defined as the last Agatston score that was recorded in the database. The change of Agatston score was calculated by subtracting baseline Agatston score from final Agatston score

Statistical analysis

Continuous variables were expressed as median (25-75 quartiles) or mean ± standard deviation (SD), categorical variables were expressed as percentages. Categorical variables were compared by Chi square test and continuous variables were compared by Student T test or Mann Whitney U test. Normality analysis was done by Kolmogorov-Smirnov or Shapiro-Wilk tests. Linear regression analysis was used to determine independent variables that affect the change in Agatston score. Regression model consisted of classical cardiovascular risks (age, gender, hypertension, diabetes, hyperlipidemia) plus baseline Agatston score. Significance threshold was selected as $p<0.05$ in all analyses. All statistical analyses were made using IBM SPSS 21.0 statistics software.

Results

Demographical and clinical data of the study population were shown in Table 1. A total of 440 patients were screened. Fourteen patients were excluded due to lack of demographical data, and 300 patients with coronary stent or coronary artery bypass surgery were excluded due to inability of Agatson score calculation. Consequently, 126 patients were involved in the final analysis. Mean age was 53.21 ± 10.82 and majority of patients were male (81.7%).

Median follow up was 36 (24-36.5) months. Baseline median Agatston score was 1.28 (0.28-53.11), final median Agatston score was 10.28 (8.50-118.50). The scatter plot of initial and final Agatston scores were shown in figure 1. The amount of change in Agatston score was 4 (4.35-49.38) and was statistically significant ($p< 0.001$).

Table 1. Characteristics of the study population

Demographical features	
Age (±SD)	53.21 ± 10.82
Gender-male n(%)	103 (81.7)
Cardiovascular risk factors n(%)	
HT	57 (45.2)
DM	24 (19.0)
HL	63 (50)
Smoking	53 (42.1)
Previous CAD	9 (7.1)
Agatston score (IQR)	
Initial	0.28 (53)*
Final	9.28 (118)*

** Change in Agatston score during follow up was statistically significant (p<0.001) (CAD: coronary artery disease, DM: diabetes mellitus, HL: hyperlipidemia, HT: hypertension)*

Sixty-three patients (50%) had zero initial Agatston score. Patients with baseline Agatston score of zero had similar cardiovascular risk factors as patients with baseline Agatston score greater than zero (Table 2).

Table 2. Subgroup analysis according to cardiovascular risks between patients with zero initial Agatston score and patients with initial Agatston score >0

Risk factors	**Initial Agatston score = 0 n:63 (50)**	**Initial Agatston score >0 n:63 (50)**	**P value**
Age	51.31 ± 6.76	48.32 ± 8.90	0.265
Gender-male	50 (79.4)	53 (84.1)	0.645
HT	29 (46.0)	28 (44.4)	1.000
HL	29 (46.0)	34 (54.0)	0.476
Smoking	30 (47.6)	23 (36.5)	0.279
Previous CAD	2 (3.2)	7 (11.1)	0.164

(CAD: coronary artery disease, DM: diabetes mellitus, HL: hyperlipidemia, HT: hypertension)

Table 3. Initial and final Agatston scores and Agatston score changes according to cardiovascular risk factor groups

	HT		DM		HL		Smoking		Previous CAD	
	yes	no	yes	no	yes	no	yes	no	yes	no
Initial Agatston score	121.41 ± 297.16*	38.87 ± 96.61 *	134.59 ± 368.97‡	62.47 ± 159.21‡	102.48 ± 262.95‡	49.93 ±1 51.26‡	58.54 ± 166.10	89.04 ± 245	249.00 ± 357.31*	62.92 ± 196.56*
Final Agatston score	211.40 ± 458.80†	76.48 ± 156.82†	243.14 ± 537.96‡	112.67 ± 264.04‡	172.94 ± 375.53	102.09 ± 287.56	118.165 ± 322.67	151.57±345.21	437.88 ± 664.36†	114.41 ± 288.02†
Agatston score change	94.08 ± 200.79*	37.69 ± 77.28 *	108.99 ± 201.45‡	52.43 ± 132.29‡	74.08 ± 154.09	52.32 ± 143.47	59.62 ± 168.65	65.80±133.48	188.88 ± 320.95†	53.53 ± 124.08†

** p=0.001 between groups; † p<0.001 between groups; ‡ p<0.05 between groups*
(CAD: coronary artery disease, DM: diabetes mellitus, HL: hyperlipidemia, HT: hypertension)

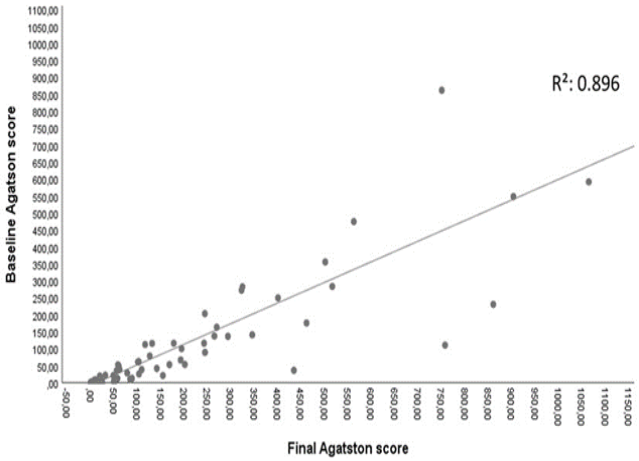

Figure 1. Scatter plot for baseline Agatston score vs. final Agatston score.

Table 4. Regression coefficients and 95% for individual predictors included in regression model for the change in Agatston score

	Regression coefficients and 95%	
Variables	**CI**	***p* value**
Age	3.57 (0.76-6.37)	0.013
Gender-male	47.52 (-17.27-112.33)	0.149
HT	28.26 (-26.93-83.45)	0.313
DM	33.47 (-30.29-97.23)	0.301
HL	2.82 (-44.20-49.86)	0.905
Smoking	30.19 (-18.36-78.74	0.221
Previous CAD	106.21 (14.42-198.01	0.024
Baseline zero Agatston score	-81.29 [(-133.89) - (-28.69)]	0.003

(CAD: coronary artery disease, DM: diabetes mellitus, HL: hyperlipidemia, HT: hypertension)

Thirteen patients (10.3%) had progressed from initial Agatston score of zero to Agatston score above zero during follow up. These patients also had similar cardiovascular risk factor profiles when compared with patients who continued to have zero Agatston scores.

When patients were categorized according to presence or absence of cardiovascular risk factors, baseline Agatston score, final Agatston score and the amount of change in Agatston score were significantly higher in patients with hypertension, diabetes or previous coronary artery disease than those without. Only baseline Agatston score was significantly higher in patients with hyperlipidemia (Table 3).

Linear regression analysis was made to determine the independent factors that affected the amount of change in Agatston score. The regression model included age, gender, hypertension, diabetes, hyperlipidemia, smoking, previous coronary artery disease and zero initial Agatston score. Age and previous coronary artery disease were significantly increased the risk of increase in Agatston score whereas zero initial Agatston score significantly decreased the risk (Table 4).

Discussion

In patients with multiple CT coronary angiograms and Agatston score measurements, we showed that age and previous coronary artery disease history were significantly affected the change in Agatston score in median 36 months.

In our study patients with hypertension, diabetes or previous coronary artery disease had significantly higher amounts of Agatston score change than the patients in corresponding risk groups.

Hypertension is a well-established risk factor for coronary heart disease (5). The association between hypertension and CAC has been investigated in recent studies. In a study by Satoh et.al, high office blood pressure and home blood pressure measurements both increased the risk for CAC in Japanese men from general population (6).

Similar to our study, several other studies found that diabetes was associated with increased CAC (7, 8). On the other hand in a recent study, Razavi et al. found that the major determinant of having an Agatston score = 0 in 10 years of follow up is younger age in a study population with diabetes (9). Similar to this finding, we showed that age was an independent predictor of Agatston score increase during follow up in our study. So it can be speculated that when it comes to calcification in coronary arteries aging is more important

than diabetes status even though diabetes was considered as a coronary artery risk equivalent.

Previous history of coronary artery disease was found to increase risk of subsequent increase in Agatston score in our study. This finding underlies the progressive nature of atherosclerotic process. However the progression of calcium does not necessarily mean the increased risk of ischemic burden. In a study by de Winter et al. 53 patients with de novo single vessel coronary artery disease were examined. Baseline CAC or progression of CAC was not associated with lower coronary hemodynamic or myocardial perfusion indices over time (10).

Another interesting finding in our study was the protective role of zero baseline Agatston score against the increase in Agatston score. In our study 13 out of 63 patients (21%) still had zero Agatston score after median 36 months of follow up. This finding is compatible with previous studies. In a recent study by Dzaye et al., 3116 participants from The MESA (Multi-Ethnic Study of Atherosclerosis) who had baseline zero Agatston score and who got rescanned after 10 years were included. The authors concluded that the warranty period of a calcium score of zero was 3-7 years depending on sex and race/ethnicity(11).

There are sevaral limitations in our study. First our study population was not randomly selected. Second female gender was under-represented. Third, anthropometric measurements such as body mass index or body surface area was not available to us. Finally, laboratory results could not be obtained.

Conclusions

In this study, age and previous coronary artery disease were independently found to increase and zero initial Agatston score was independently found to decrease the risk of Agatston score increment during median 36 months of follow up. Additional studies are needed to establish the patient specific characteristics that may affect coronary artery calcium development and progress.

Ethical Approval: *Necessary informed consent was obtained from each participant. The study protocol was approved by local ethical committee (Yeditepe University Non-interventional Clinical Trials Ethics Committee 21/06/2021 -29). Principles outlined by Declaration of Helsinki was followed throughout the study. All authors declare no conflict of interest.*

Author Contributions:
Concept: M.A.Ş., A.T.C., M.D.
Literature Review: M.A.Ş, O.Ö., Ç.K., E.D.
Design : M.A.Ş., A.T.C., M.D.
Data acquisition: M.A.Ş., A.T.C, M.D.
Analysis and interpretation: M.A.Ş., O.Ö., Ç.K.
Writing manuscript: M.A.Ş., A.T.C., Ç.K., E.D.
Critical revision of manuscript: O.Ö., M.D.

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