JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.974676
J Contemp Med 202x;xx(x):xxx-xxx

Orjinal Araştırma / Original Article

B-Type Natriuretic Peptide and Calcium Score in Angina Pectoris Patients

Angina Pektoris Hastalarında B-Tipi Natriüretik Peptit ve Kalsiyum Skoru

Özlem Özbek[1], Hüseyin Oğuz Caymaz[2]

[1]Haseki Training and Research Hospital, Department of Cardiology, Istanbul, Turkey
[2]Marmara University Faculty of Medicine, Department of Cardiology, Istanbul, Turkey

Abstract

Objective: The purpose of this study is to look into the relationship between coronary artery disease evaluated with multislice computed tomography (MSCT) findings and B-type natriuretic peptide (BNP) and calcium score (CaS).

Material and Method: The study included 83 patients who were administered to our center and who had asymptomatic and stable angina pectoris. Blood samples were collected for BNP testing, and the Abbott AxSYM System kit was used for measurements. Calcium scoring was performed on each of the four main coronary arteries, and the total "Agatston" score was calculated for each patient by summing up the results. MSCT angiograms were studied at the three-dimensional operating base.

Results: Coronary artery disease (CAD) was found in 51 (61.4%) patients, while the coronary arteries of 32 (38.6%) patients were deemed normal. While patients with CAD had a median BNP of 33.9 (0–834), those without CAD had a median of 19.2 (0–185), which was statistically significant (p=0.011). Furthermore, there was a positive correlation between the number of vessels involved and BNP (r = 0.364, p=0.001). BNP levels were found to be significantly higher in hypertensive patients (p=0.008). The CaS and BNP median of the group with three-vessel involvement were significantly higher (p < 0.001 and p=0.007, respectively). According to the multivariate logistic regression results, BNP and age were not found to be associated with presence of CAD, but CaS was found to be associated.

Conclusion: CaS was found to be associated with presence of CAD. Further studies should be conducted to confirm aforementioned associations.

Keywords: Coronary artery disease, B-type natriuretic peptide, Coronary artery calcium

Öz

Amaç: Bu çalışmanın amacı, çok kesitli bilgisayarlı tomografi (ÇKBT) bulguları ile değerlendirilen koroner arter hastalığı ile B tipi natriüretik peptit (BNP) ve kalsiyum skoru (KaS) arasındaki ilişkiyi incelemektir.

Gereç ve Yöntem: Merkezimize başvuran asemptomatik ve stabil angina pektorisli 83 hasta çalışmaya alındı. BNP testi için kan örnekleri alındı ve ölçümler için Abbott AxSYM Sistem kiti kullanıldı. Dört ana koroner arterin her biri için kalsiyum skorlaması yapıldı ve sonuçlar toplanarak her hasta için toplam "Agatston" skoru hesaplandı. ÇKBT anjiyogramları, üç boyutlu işlem tabanında çalışıldı.

Bulgular: 51 (%61,4) hastada koroner arter hastalığı (KAH) saptanırken, 32 (%38,6) hastanın koroner arterleri normaldi. 17 hastada (%20,5) tek damar tutulumu, 18 hastada (%21,7) iki damar tutulumu, 16 hastada (%19,3) üç damar tutulumu saptandı. KAH olan hastaların medyan BNP'si 33,9 (0-834) iken, KAH olmayanların medyan değeri 19,2 (0-185) idi ve bu istatistiksel olarak anlamlıydı (p=0,011). Ayrıca tutulan damar sayısı ile BNP arasında pozitif bir korelasyon vardı (r = 0,364, p=0,001). Hipertansif hastalarda BNP düzeyleri anlamlı olarak yüksek bulundu (p=0,008). Üç damar tutulumu olan grubun KaS ve BNP medyanı anlamlı olarak daha yüksekti (sırasıyla p<0,001 ve p=0,007). Çok değişkenli lojistik regresyon sonuçlarına göre BNP ve yaş KAH varlığı ile ilişkili bulunmazken CaS ilişkili bulundu.

Sonuç: CaS, KAH varlığı ile ilişkili bulundu. Yukarıda belirtilen ilişkileri doğrulamak için daha fazla çalışma yapılmalıdır.

Anahtar Kelimeler: Koroner arter hastalığı, B tipi natriüretik peptit, Koroner arter kalsiyum

Corresponding *(İletişim)*: Özlem Özbek, Department of Cardiology, Haseki Training and Research Hospital, Istanbul, Turkey
E-mail *(E-posta)*: drozle@hotmail.com
Received *(Geliş Tarihi)*: 26.07.2021 **Accepted *(Kabul Tarihi)*:** 26.09.2021

INTRODUCTION

Cardiovascular diseases consist of ischemic heart disease, stroke, heart failure, peripheral artery disease, and a variety of other cardiac and vascular conditions. These diseases are among the leading causes of death and morbidity worldwide, with ischemic heart disease being the leading cause of death in countries of all income groups.[1,2]

Multislice computed tomography (MSCT) angiography is a noninvasive screening method used to diagnose coronary artery atherosclerosis.[3] Moreover, MSCT coronary angiography has become more popular in recent years. In addition, it has been reported that it outperforms the standard invasive method in the evaluation of some parameters such as the degree of calcification.[4]

Evaluation of coronary artery calcification by computed tomography is equivalent to the total coronary atherosclerosis burden and cardiovascular event risk.[5] The Agatston method is the most widely used for calculating the calcium score (CaS).[6] CaS has been shown to be an independent risk marker for cardiac events, cardiac mortality, and all-cause mortality, and it adds prognostic information to other cardiovascular risk markers.[7]

B-type natriuretic peptide (BNP) is another parameter whose level increases in heart failure caused by several heart diseases, including ischemic heart disease, and is used as a prognostic indicator.[8] In addition to BNP elevation having a prognostic value, a decrease in BNP levels during hospital follow-up was also used as an indicator of a favorable prognosis.[9] Although MSCT and BNP levels and CaS are used in the evaluation of coronary artery diseases (CAD), there have been few studies that compare the two.

The purpose of this study is to investigate the relationship between coronary artery disease as determined by MSCT findings and BNP and CaS.

MATERIAL AND METHOD

The study was approved by the Research Ethics Committee of Marmara University Faculty of Medicine (No: B.30.2.MAR.0.01.00.02/AEK-258). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients

The study included 83 patients who were administered to our center between September 1, 2006, and December 21, 2006. After being informed about the aim of the study, all patients provided written informed consent.

Inclusion Criteria

The study included patients with asymptomatic and stable angina pectoris.

Exclusion Criteria

1. Patients who refuse to participate in the study
2. With mental/physical disabilities who are unable to provide written consent
3. Those who have an atrial fibrillation rhythm
4. Those suffering from chronic obstructive pulmonary disease
5. Who have had myocardial infarction, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft
6. Those who describe unstable angina pectoris

Measurements

Just prior to the shooting, vascular access was established in the right arm. Blood samples were collected for BNP and high-sensitivity C-reactive protein (hsCRP) using Abbott AxSYM System kit for measurements.

After the image for calcium scoring (Agatston) was taken, 90 cc of nonionic contrast material was administered, and the shooting was completed within 10 seconds. The topogram image was obtained while the patient was lying in supine position. Then, to minimize heart movements, all examinations were performed, including the whole heart from the aortic root, with a breath-holding time of 3–5 seconds and ECG triggering at 80% R-R interval.

Four major coronary arteries were examined for the presence of calcified lesions throughout their traces: the left main artery, left anterior descending (LAD) artery, circumflex artery (Cx), and right coronary artery. All numerical data with homogeneous variances were evaluated: systolic tension arterial (STA), diastolic tension arterial, heart rate, left ventricular ejection fraction, interventricular septum end-diastolic thickness, interventricular septum end-systolic thickness, lateral septum end-diastolic thickness, lateral septum end-systolic thickness, pulmonary vein mean diameter (PVMD), right pulmonary artery diameter, and left pulmonary artery diameter.

The "Agatston" score was calculated for calcification in the coronary arteries using the SYNGO software (Siemens Medical Systems). According to the scoring system, lesions with a CT density of more than 130 HU in 2–3 pixels adjacent to each other, in an area larger than 1 mm2, were interpreted as calcification. The CaS was calculated for each calcified lesion by multiplying the lesion area by the intensity score determined by lesion density. Calcium scoring was performed on each of the four main coronary arteries, and the total "Agatston" score was calculated for each patient by adding the scores.[6]

MSCT angiograms were studied at the three-dimensional operating base (Aquarius, TeraRecon, San Mateo, California).

The participants in the study were divided into two groups: those who had CAD and those who did not. In addition, they were also divided into four groups (normal coronary arteries, single-vessel involvement, two-vessel involvement, and three-vessel involvement) based on the number of vessels involved.

Statistical Analysis

For the analyses, SPSS v20 (SPSS Inc., Chicago, IL, USA) was used. The Shapiro-Wilk test was used to determine the normality. According to the normality check, data are presented as mean ± standard deviations or median (minimum-maximum) for continuous variables and as frequency (percentage) for categorical variables. While normally distributed variables were analyzed using the student t-test and one-way ANOVA test, non-normally distributed variables were analyzed using the Mann-Whitney U test and Kruskal-Wallis H test. Moreover, the chi-square tests or Fisher's exact tests were used to analyze categorical variables. To evaluate the relationships between continuous variables, Spearman correlation coefficients were calculated. Multivariate logistic regression model were constructed. The dependent variable was presence of CAD. Independent variables were selected from the factors showed statistically significant relationship with presence of CAD. In addition, p<0.05 was regarded as statistically significant.

RESULTS

The study group consisted of 59 (71.0%) men and 24 (29.0%) women, with a mean age of 52.6 ± 12.5.

All patients had a median BNP of 31.1 pg/ml (0–834). Moreover, male patients had a median BNP of 30.9 pg/ml (0–693), whereas female patients had a median BNP of 39.0 pg/ml (0–834), (p=0.227). The hsCRP median was 1.8 mg/l (0.3–19.0). **Table 1** shows some characteristics of the study group.

Table 1. Distribution of some characteristics of men and women

	Male	Female	Total	p
Age	49.0 (25-89)	56.5 (40-81)	50.0 (25-89)	0.004
BMI (kg/m^2)	26.7 (21.3-37.9)	26.6 (22.1-35.2)	26.6 (21.3-37.9)	0.726
BNP (pg/ml)	30.9 (0-693)	39.0 (0-834)	31.1 (0-834)	0.227
hsCRP (mg/l)	1.7 (0.3-19.0)	2.1 (0.4-14.3)	1.8 (0.3-19.0)	0.713
Smoking history	33 (78.6%)	9 (21.4%)	42 (100%)	0.128
Hyperlipidemia history	33 (71.1%)	13 (28.3%)	46 (100%)	0.883
Hypertension history	27 (60.0%)	18 (40.0%)	45 (100%)	0.015
Diabetes Mellitus history	11 (64.7%)	6 (35.3%)	17 (100%)	0.515

While CAD was detected in 51 (61.4%) patients, the coronary arteries of 32 (38.6%) patients were found to be normal. Single-vessel involvement was detected in 17 (20.5%) patients, two-vessel involvement in 18 (21.7%) patients, and three-vessel involvement in 16 (19.3%) patients. The most involved artery was the LAD. Furthermore, 18 (21.7%) patients had exertional angina. When BNP, hsCRP, and CaS levels in patients with exertional angina were compared, all three were found to be significantly higher than asymptomatic patients (p=0.020, p=0.034, and p=0.008, respectively).

The median age of patients with CAD was 53.0 (36–89), which was significantly higher than those without CAD (p=0.002). When the number of vessels involved was considered, the median age of the group with three-vessel involvement was significantly higher than the group without CAD (p=0.002).

While the median BNP of patients with CAD was 33.9 (0–834), those without CAD had a median of 19.2 (0–185) (p=0.011). In addition, there was a positive correlation between the number of vessels involved and BNP (r=0.364, p=0.001). The relationship between BNP level and smoking, hyperlipidemia, hypertension, and DM history was also investigated. While BNP levels were found to be significantly higher in hypertensive patients (p=0.008), there was no significant difference between other variables and BNP levels (p>0.05 for each).

CaS values ranged from 0.0 to 1471.0. The CaS mean was 104.6 ± 240.5 (median value 0.0). Further, CaS was measured above 0 in 41 patients. The median CaS of patients with CAD was 48.9 (0–1471), which was significantly higher than those without CAD (p<0.001). When the number of vessels involved was considered, the CaS median of the group with three-vessel involvement was significantly higher than the other groups (p<0.001). In terms of median hsCRP, there was no significant difference between groups (p=0.222). **Table 2** and **Table 3** show some characteristics of the study group.

According to the multivariate logistic regression analysis, only factor affecting the CAD was found to be as CaS (p=0.049). BNP and age were found to be non-significant in multivariate analysis (**Table 4**).

Table 2. The distribution of some characteristics of the study group according to whether they have CAD or not.

	CAD absence	CAD presence	p
Age	47.0 (25.0-68.0)	53.0 (36.0-89.0)	0.002
BMI	26.7 (24.2-37.2)	26.5 (21.3-37.9)	0.438
BNP	19.2 (0-185)	33.9 (0-834)	0.011
CaS	0 (0-38.0)	48.9 (0-1471)	<0.001
hsCRP	1.5 (0.3-19.0)	1.9 (0.4-15.0)	0.222
STA	139.2±14.6	140.4±20.7	0.763
DTA	81.1±11.0	80.7±10.5	0.849
HR	73.5±9.2	71.1±8.6	0.228
LVEF	57.5±6.9	57.1±7.9	0.828
ISEDT	10.3±1.5	10.9±1.6	0.090
ISEST	13.4±1.5	13.8±1.8	0.334
LSEDT	9.6±1.6	9.8±2.2	0.618
LSEST	14.8±2.1	15.4±3.1	0.388
PVMD	12.7±1.4	13.2±1.5	0.181
RPAD	20.9±2.6	21.7±2.6	0.191
LPAD	21.2±1.9	21.5±2.6	0.639

Table 3. The distribution of some characteristics of the study according to the number of vessels involved.

	CAD absence	single-vessel involvement	2-vessels involvement	3-vessels involvement	p
Age	47.0 (25.0-68.0	49.0 (37.0-69.0)	50.5 (36.0-81.0)	62.0 (41.0-89.0)	0.002
BMI	26.7 (24.2-37.2)	24.9 (21.3-33.3)	27.3 (23.2-37.9)	27.3 (22.6-36.6)	0.369
BNP	19.2 (0-38.0)	26.3 (0-235)	31.0 (0-403)	86.6 (10.6-693)	0.007
CaS	0 (0-38.0)	0 (0-158)	52.6 (0-403)	201.7 (2.9-1471)	<0.001
hsCRP	1.5 (0.3-19.0)	1.8 (0.4-11.7)	2.6 (0.6-15.0)	1.6 (0.8-7.4)	0.334
STA	139.2±14.6	131.2±17.9	140.0±22.4	150.8±17.6	0.023
DTA	81.1±11.0	77.0±10.4	83.6±12.0	81.4±7.8	0.323
Nds	73.5±9.2	68.7±8.4	72.1±7.4	72.5±9.9	0.352
LVEF	57.5±6.9	59.1±5.7	56.9±7.1	54.3±11.1	0.436
ISEDT	10.3±1.5	10.6±1.7	11.3±1.1	10.9±2.0	0.244
ISEST	13.4±1.5	13.6±2.0	14.2±1.7	13.8±1.9	0.617
LSEDT	9.6±1.6	9.5±2.8	9.9±1.6	10.1±2.3	0.838
LSEST	14.8±2.1	15.0±3.8	16.0±1.5	15.1±3.8	0.585
PVMD	12.7±1.4	12.4±0.8	13.9±1.7	13.5±1.4	0.021
RPAD	20.9±2.6	20.8±1.5	21.5±2.0	23.3±4.0	0.069
LPAD	21.2±1.9	21.3±2.6	21.2±2.9	22.7±2.2	0.684

Table 4. Multivariate regression results for the factors affected the coronary artery disease

	B	S.E.	Sig.	Exp(B)	95% CI for EXP(B)	
					Lower	Upper
Age	0.034	0.032	0.299	1.034	0.971	1.102
BNP	0.002	0.004	0.725	1.002	0.993	1.010
CaS	0.087	0.044	0.049	1.091	1.000	1.190
Constant	-2.201	1.551	0.156	0.111		

Dependent variable: Presence of CAD, Nagelgerke R2: 0.507

DISCUSSION

In this study, we analyzed 83 patients who had asymptomatic or stable angina pectoris and had their cardiac findings evaluated with MSCT. The following were the major findings:(1) CAD was found in 51 (61.4%) of the patients. (2) Those with CAD had significantly higher BNP levels. (3) There was a positive correlation between the number of vessels involved and BNP. (4) BNP levels were found to be significantly higher in hypertensive patients. (5) CaS levels were higher in CAD patients. (6) Exertional angina patients had higher levels of BNP, hsCRP, and CaS than asymptomatic patients.(7) Multivariate analysis showed CaS levels were associated with presence of CAD, but BNP were not.

In recent studies, many mechanisms, including myocardial ischemia, have been shown to contribute to BNP release, and BNP level has also been shown to be a useful clinical indicator in the diagnosis and prognosis of cardiovascular diseases.[10-13] Furthermore, it has been reported that BNP has vasodilator effects on the coronary artery system and that BNP primarily acts on both epicardial coronary arteries and coronary microvessels.[10,12] Due to its release in response to increased wall tension, it represents a higher degree of myocardial dysfunction in acute coronary syndrome patients with low left ventricular ejection rate and high BNP levels, with a high risk of congestive heart failure and mortality.[14] BNP level was found to be higher, particularly in patients with three-vessel involvement. In addition, when compared to asymptomatic patients, BNP levels were significantly higher in patients with exertional angina. However in multivariate analysis, there was no significant relationship between CAD and BNP.

For a long time, there has been a relationship between hypertension and CAD. In the current study, the STA of patients with three-vessel involvement was significantly higher than in patients with single-vessel involvement. Furthermore, those with a history of HT had higher BNP levels.

The presence of calcium in the coronary arteries indicates the presence of atherosclerosis, and the extent of coronary calcium corresponds to the burden of atherosclerotic plaque.[15-17] In addition, in asymptomatic individuals, coronary artery calcification has been shown to be the most predictive cardiovascular risk marker.[18,19] A study found that when CaS is added to traditional risk factors, it improves risk stratification for the prediction of coronary disease events in an asymptomatic population.[20] In symptomatic patients, the CaS score can be interpreted as a screening tool to facilitate diagnosis. Therefore, it was reported that using CaS score alone in symptomatic patients is limited.[7] During an 11-year follow-up in a population-based study of older adults without known cardiovascular disease, individual coronary artery calcium score was shown to provide better discrimination than chronological age for atherosclerotic coronary heart disease.[21] In our study, total CaS was found to be greater than 0 in 38 (71.6%) of those with CAD. In addition, CaS was found to be significantly higher in CAD patients with three-vessel involvement. Also, CaS was found to be associated with presence of CAD in multivariate logistic regression analysis. The results confirm that a high level of CaS is associated with the presence and severity of CAD. However, values greater than 0 in some patients with normal coronary arteries indicate that total CaS may not be a reliable predictor of the presence of CAD.

There were several limitations in this study. First, our results were limited to the experience of a single center, and the sample size was relatively small. Second, in this study, only circulating BNP levels were measured. Measuring plasma BNP levels in the coronary sinus may have been more precise in determining the relationship between BNP level and CAD. Third, changes in CaS resulting from medical treatment and/or lifestyle changes were not evaluated in this study. Therefore, these changes may have influenced the results.

CONCLUSION

CAD was detected in more than half of the study participants. The most involvement was determined to be from a single-vessel, with LAD being the most involved vessel. CaS levels were significantly higher in those with CAD, and there was a positive correlation between the number of vessels involved and BNP. Further studies should be performed to confirm these conclusions.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Research Ethics Committee of Marmara University Faculty of Medicine (No: B.30.2.MAR.0.01.00.02/AEK-258)

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: This study was funded by Sonomed. They provided the kits (4400 TL) and free labaratuary usage to measurements of BNP and hsCRP.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Nowbar AN, Gitto M, Howard JP, Francis DP, Al-Lamee R. Mortality from ischemic heart disease: Analysis of data from the World Health Organization and coronary artery disease risk factors From NCD Risk Factor Collaboration. Circ Cardiovasc Qual Outcomes 2019;12(6):e005375.
2. Mensah GA, Roth GA, Fuster V. The global burden of cardiovascular diseases and risk factors: 2020 and beyond. American College of Cardiology Foundation Washington, DC; 2019.
3. Kishi S, Magalhaes TA, Cerci RJ, et al. Total coronary atherosclerotic plaque burden assessment by CT angiography for detecting obstructive coronary artery disease associated with myocardial perfusion abnormalities. J Cardiovasc Comput Tomogr 2016;10(2):121-7.
4. Shumakov I, Sukhova M. MSCT Coronary Angiography in Diagnosis of Chronic Coronary Occlusions. Современные технологии в медицине 2018;10(2):118-24.
5. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 2006;114(16):1761-91.
6. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15(4):827-32.
7. Neves PO, Andrade J, Monção H. Coronary artery calcium score: current status. Radiol Bras 2017;50(3):182-9.
8. Morrow DA, De Lemos JA, Sabatine MS, et al. Evaluation of B-type natriuretic peptide for risk assessment in unstable angina/non–ST-elevation myocardial infarction: B-type natriuretic peptide and prognosis in TACTICS-TIMI 18. J Am Coll Cardiol 2003;41(8):1264-72.
9. Kagiyama N, Kitai T, Hayashida A, et al. Prognostic value of BNP reduction during hospitalization in patients with acute heart failure. J Card Fail 2019;25(9):712-21.
10. Itakura R, Inoue Y, Ogawa K, et al. A highly-sensitized response of b-type natriuretic peptide to cardiac ischaemia quantified by intracoronary pressure measurements. Sci Rep 2020;10(1):1-11.
11. Berthelot E, Mas R, Damy T, et al. NTproBNP and BNP level in acute heart failure patients aged 75 or older are higher than in non-cardiac dyspnoea. Arch Cardiovasc Dis 2020;12(1):44.
12. Goetze JP, Bruneau BG, Ramos HR, Ogawa T, De Bold MK, Adolfo J. Cardiac natriuretic peptides. Nat Rev Cardiol 2020;17(11):698-717.
13. Al Awadi M, Eltahlawi M, Gad M, Ismail H. Prognostic Value of Serum BNP in Patients with NSTEMI and Its Correlation with Extent of Coronary Artery Disease. Zagazig University Med J 2021.
14. Nagaya N, Nishikimi T, Goto Y, et al. Plasma brain natriuretic peptide is a biochemical marker for the prediction of progressive ventricular remodeling after acute myocardial infarction. Am Heart J 1998;135(1):21-8.
15. Arnson Y, Rozanski A, Gransar H, et al. Comparison of the coronary artery calcium score and number of calcified coronary plaques for predicting patient mortality risk. Am J Cardiol 2017;120(12):2154-9.
16. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area: a histopathologic correlative study. Circulation 1995;92(8):2157-62.
17. Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using nondecalcifying methodology. J Am Coll Cardiol 1998;31(1):126-33.
18. Greenland P, Blaha MJ, Budoff MJ, Erbel R, Watson KE. Coronary calcium score and cardiovascular risk. J Am Coll Cardiol 2018;72(4):434-47.
19. Budoff MJ, Young R, Burke G, et al. Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA). Eur Heart J 2018;39(25):2401-8.
20. Polonsky TS, Mcclelland RL, Jorgensen NW, et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. JAMA 2010;303(16):1610-6.
21. Yano Y, O'donnell CJ, Kuller L, et al. Association of coronary artery calcium score vs age with cardiovascular risk in older adults: an analysis of pooled population-based studies. JAMA Cardiol 2017;2(9):986-94.