

Evaluation of the atherosclerotic plaque of coronary arteries: A 10-year epidemiological surveillance study

Mohammad Zahedi¹, Mahdie Darvish Khezri¹, Amirhossein Hessami², Ali Akbar Rezaei¹, Fatemeh Amuzad¹, Parham Mortazavi³, Samere Asadpour¹, Soheil Azizi^{4,5*}

1 Department of Medical Laboratory Sciences, Student Research Committee, School of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran.

2 Student Research Committee, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran,

3 Student Research Committee, School of pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.

4 Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran.

5 Cardiovascular Research center, Mazandaran University of Medical Sciences, Sari, Iran.

***Corresponding Author: Soheil Azizi, Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran.**

 : [+989111119989](tel:+989111119989)

 : soheil_azizi@yahoo.com

Abstract

Background: Coronary arteries are the main vessels supplying the heart. Various factors can affect their performance, which causes coronary diseases and impaired blood supply and irreparable complications. Coronary artery disease (CAD) is one of the most common cardiovascular diseases with the highest mortality rate and disability among patients. The objective of this study is to investigate the epidemiological and anatomical characteristics of the atherosclerotic plaques in coronary arteries and their risk factors in Mazandaran Heart Center.

Method: This cross-sectional study with a census design performed on all patients with atherosclerotic plaque, who undergone atherectomy surgery, from November 2009 to January 2019. Patient's information was extracted from their medical records archive with ethical points. SPSS 16.0 was used for statistical analysis.

Result: Out of 156 patients with atherosclerotic plaque, 60.9% were male. The mean age of patients was 61.58 ± 8.9 years. The most incidence of atherosclerotic plaques was seen in 50-80 age category. Atherosclerotic plaques were mostly found in the right coronary (RCA) (53.8%) followed by left anterior descending (LAD) (41%) arteries, which was more common in men. No significant relationship was observed between sex, age, the number of arteries involved and level of biochemical variables.

Conclusion: We found that gender, age, calcification, FBS, TG, TC, HDL, and LDL do not have significant effect on "site" of plaque in different coronary arteries which might due to same physiological and histological structure of these arteries. Further studies are being needed for etiology and mechanism involved.

Key Word:

Coronary arteries,
atherosclerotic plaque,
heart disease, risk factor

Introduction

Cardiovascular diseases are one of the significant causes of death in Iran (1). One of the most common cardiovascular diseases with the highest mortality rate and disability

among patients is coronary artery disease (CAD) (2). Atherosclerosis is known as a chronic inflammatory disease with systemic manifestations

that lead to CAD in a majority of cases. Atherosclerotic plaque is a major feature of this disease which causes vascular stenosis and reduces blood flow gradually. Atherosclerotic plaque disorders may ultimately lead to acute myocardial infarction, sudden cardiac death and, acute coronary syndromes among most patients (3). Previous studies show that atherosclerosis begins in the first days of life. The prevalence of this disease increases in childhood and slowly progresses so that it has become one of the significant causes of death among young people and adults. Therefore, this disease takes a long hidden period to become a complete clinical disease such as stroke or other cardiovascular diseases (4). Plaque is a strong predictor of cardiovascular disease (5). It is caused by sedimentation of substances such as calcium, cholesterol, fiber, and cellular appendages which causes vascular stenosis (6). When lipids and other substances are sedimented and accumulated inside vessels, they are in shape of narrow stands and stains that gradually progress and cause narrowing of vessels and limiting blood flow (3). Tearing of plaque's shell and bleeding wall is a hazardous condition because it leads to blood clots (6). Calcification has the potential of being shaped in atherosclerotic plaques and associated with the severity of the disease, which can be used as a screening test for asymptomatic patients (7).

Age, family history of premature CAD,

history of cigarette smoking, hypertension, menopause, diabetes, hypercholesterolemia, high LDL cholesterol, low HDL cholesterol, hypertriglyceridemia, different genotypes of Apolipoprotein E increase the risk of CAD (2, 8, 9). One of the most common diagnostic methods is angiography; however, this method is associated with some complications such as hemorrhage, hematoma, distal embolism, and arterial thrombosis although they can be prevented from occurring with enough rest (10).

Some factors can have direct and indirect effects on the risk of coronary artery diseases and reducing mortality such as exercise, not smoking, normal blood pressure, normal blood glucose level, normal total cholesterol level, keeping normal weight and healthy diet (2). According to all advances in medical science and facilitation of the diagnosis and treatment of vascular diseases, there is still no significant improvement in seasonable diagnosis, cure, and reduction of postoperative complications of coronary plaque so, the prevalence of this disease and mortality are rising in Iran. The purpose of this study is to evaluate the epidemiologic and anatomic of coronary plaques in patients who were hospitalized in Mazandaran Heart Center, Sari, Iran.

Materials and Methods

This cross-sectional study with a census design was performed on all of the patients with atherosclerotic plaque, who had undergone atherectomy surgery, from November 2009 to January 2019 in Mazandaran Heart Center, teaching hospital affiliated to Mazandaran University of Medical Science in Sari, Mazandaran, Iran.

Overall, 156 patients with atherosclerotic plaque undergoing atherectomy surgery participated in our investigation. Patient's information was extracted from their medical records archive with ethical points using a self-made checklist. The checklist contains variables, including demographic features (age, gender), biochemical, and pathology test results. All data were obtained from computerized records and manual archives of the hospital. Inclusion criteria included medical records of all patients with atherosclerotic plaque, who undergone atherectomy surgery and exclusion criteria of the study were the incomplete medical records, patient without atherosclerotic plaque, and patient with carotid plaque.

At the first, Microsoft excel 2016 was used to categorize the extracted data, Statistical Package for the Social Sciences 16.0 (SPSS 16.0 Inc. Chicago, IL, USA) was used for statistical analysis using Chi-squared, Kolmogorov-Smirnov and Mann-Whitney tests. The significant level for

P-value was set at 0.05.

Ethical consideration

Ethics committee of Mazandaran University of Medical Sciences (MAZUMS) approved the study by code IR.MAZUMS.REC.1398.002 which adopted on Feb 20, 2018. A request has been sent by study team to Mazandaran Heart Center to approve collaboration. In order to comply with ethical standards, all information contained in the medical records archive was used confidentially and, exclusively for the aim of this study and all files were delivered to the Archive without any changes.

Results:

Out of 156 patients with atherosclerotic plaque, 60.9% were male. The mean age of patients was 61.58 ± 8.9 years and most of the patients were in the 60-70 age category. The most incidence of atherosclerotic plaques has been observed in the age category of 60-70 (41%), 50-60 (34.6%) and 70-80 (12.2%), respectively. Atherosclerotic

plaques were mostly found in the right coronary (RCA)(53.8%) followed by left anterior descending (LAD) (41%) arteries, which was more common in men. The distribution of atherosclerotic plaque and coronary artery involved patient and age category and gender is also shown in Table 1 and Table 2, respectively.

Table 1. The Distribution and association of coronary arteries involved in patients by age category

| Age category (years) | LAD | OM | RCA | PDA | LCX | RCX | |
|----------------------|----------|----------|------------|----------|----------|----------|------------|
| 30-40 | 1 | 0 | 1 | 0 | 0 | 0 | 2 (1.3%) |
| 40-50 | 6 | 0 | 8 | 0 | 0 | 0 | 14 (9%) |
| 50-60 | 24 | 0 | 28 | 0 | 1 | 1 | 54 (34.6%) |
| 60-70 | 28 | 1 | 32 | 2 | 1 | 0 | 64 (41%) |
| 70-80 | 5 | 0 | 13 | 0 | 1 | 0 | 19 (12.2%) |
| 80-90 | 0 | 0 | 1 | 1 | 0 | 0 | 2 (1.3%) |
| >90 | 0 | 0 | 1 | 0 | 0 | 0 | 1 (0.6%) |
| Total | 64 (41%) | 1 (0.6%) | 84 (53.8%) | 3 (1.9%) | 3 (1.9%) | 1 (0.6%) | 156 (100%) |
| P-Value | 0.632 | 0.963 | 0.805 | 0.000 | 0.957 | 0.929 | |

*P-value below 0.05 is considered significant.

PDA;(Posterior Descending Artery), OM;(obtuse marginal), LCX;(left circumflex artery), RCX;(ramus circumflexis)

Table 2. The distribution and association of coronary artery involved in patient by gender

| Artery involved Gender | LAD | | OM | | RCA | | PDA | | LCX | | RCX | |
|---------------------------|---------------|---------------|-------------|-------------|---------------|---------------|-------------|-------------|-------------|-------------|-------------|-------------|
| | F | M | F | M | F | M | F | M | F | M | F | M |
| No. (%) | 26 (16.7%) | 38 (24.4%) | 0 (0.0%) | 1 (0.6%) | 30 (19.2%) | 54 (34.6%) | 3 (1.9%) | 0 (0.0%) | 2 (1.3%) | 1 (0.6%) | 0 (0.0%) | 1 (0.6%) |
| Total | 64 (41%) | | 1 (0.6%) | | 84 (53.8%) | | 3 (1.9%) | | 3 (1.9%) | | 1 (0.6%) | |
| P-value | 0.745 | | 0.421 | | 0.349 | | 0.029* | | 0.323 | | 0.421 | |

*P-value below 0.05 is considered significant.

The coronary calcification in RCA arteries was more than LAD arteries. In most cases, calcification of LAD artery was patchy (37.6 %) and in RCA artery was massive (38.1%). In LCX

artery, calcification was most patchy (66.6%). The distribution of coronary calcification is also shown in Table 3.

Table 3. The distribution and association of coronary artery sclerosis and calcification

| No. (%) | LAD | OM | RCA | PDA | LCX | RCX |
|----------------|------------|----------|------------|----------|----------|----------|
| Patchy | 24 (15.4%) | 0 (0.0%) | 28 (17.9%) | 1 (0.6%) | 2 (1.3%) | 1 (0.6%) |
| Massive | 21 (13.5%) | 0 (0.0%) | 32 (20.5%) | 2 (1.3%) | 0 (0.0%) | 0 (0.0%) |
| None | 19 (12.2%) | 1 (0.6%) | 24 (15.4%) | 0 (0.0%) | 1 (0.6%) | 0 (0.0%) |
| Total | 64 (41.0%) | 1 (0.6%) | 84 (53.8%) | 3 (1.9%) | 3 (1.9%) | 1 (0.6%) |
| P-value | 0.866 | 0.289 | 0.686 | 0.418 | 0.385 | 0.407 |

The mean level of Fasting Blood Sugar (FBS), Triglycerides (TG), Total Cholesterol (TC), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL) were 153, 151, 165, 37, 94 (mg/dl), respectively.

No significant relationship has been observed between sex, age, the number of arteries involved and level of biochemical variables.

We found that FBS, TG, TC, HDL, and LDL do not have any significant association with atherosclerosis in different coronary arteries. It is recommended to check more factors in further studies and specific factors may even effect on this disease in different regions due to race.

Discussion:

In the present study, we report different variables affecting atherosclerosis of coronary artery. One of the risk factors which is associated with cardiovascular diseases (CVD) is age (11). It is estimated that about one-fifth world population will be aged 65 or older by 2030, causing an increase in CVD (12). In previous studies mean age of patients with coronary artery disease estimated 63.3 ± 9 and male patients were more than female (13) the same as our study. The prevalence of ischemic heart disease rises from 290 in 100000 for 40 to 44 years old and reaches its highest number for 75 to 79 years of age and declines slightly for those with 80 years of age

(14) which has the same pattern to our study. Age and sex are among the conventional risk factors of coronary artery disease (15). Previous study's results showed that women have lower coronary artery calcification and lower coronary artery disease prevalence (16). This could be due to the protective effect of estrogen in premenopausal women (17). By contrast, Menopause is a certain risk factor for cardiovascular disease (18), which might be due to a high level of LDL during menopause (19). The study by Kardys et al. (20) investigated vascular bed differences in both genders and showed that coronary calcium scores and intima-media thickness was higher in men than women (OR:4.4 and OR:2.6, respectively). Meanwhile in our study, there was no significant correlation between atherosclerosis in different coronary arteries (RCA, LAD, PDA, RCX, LCX and OM) with gender same as the study by Soe Hee Ann et al. (21) and age. It seems that the site of plaques does not have any significant difference between genders and different age groups and further studies needed in this case for etiology. Almost 40-50% of coronary artery calcification are related to genetics (22). Patients with atherosclerosis of coronary artery have higher coronary calcium scores (23). Previous studies showed that calcification of coronary arteries was present more frequently in left anterior descending artery and then followed by left circumflex branch

and right coronary artery, respectively (24). In our study calcification of coronary artery observed in left anterior descending most frequently same as previous study and then followed by right coronary artery and left circumflex artery respectively but there was no significant difference between distribution, note that p-values were not reported in previous study by Frink et al. (24) so further studies are being needed. The formation of atherosclerosis in coronary arteries is related to wall stiffness. A study by Ohayon et al. (25) investigated luminal atrial wall stretch and stiffness in patients with minimal coronary artery disease showed that plaques in coronary arteries are subjected to high luminal atrial wall stretch and stiffness. Left main coronary artery had slightly more stiffness than left anterior descending and left circumflex arteries (25). Association between cholesterol levels with coronary heart disease (CHD) mortality has been reported in different populations (26). Previous studies demonstrated that total plasma cholesterol and LDL-C were directly associated with coronary heart disease (15) and a high level of triglycerides are independently associated with increased risk of CVD (27). In previous studies on HDL cholesterol effect on CHD, participants with low HDL profiles are at risk CHD almost twice than people with optimal lipid level (all variables adjusted, HR:2.25, P-value < 0.001) (28). Meanwhile, our results showed that there is no significant association

between “site” of plaque in different coronary arteries and biochemical variables including LDL, HDL, Total cholesterol and triglycerides which can suggest that high level of LDL or low level of HDL can affect different coronary arteries.

Results of our study showed that there are no significant associations between age, gender, calcification and biochemical variables with atherosclerosis in different coronary arteries (RCA, LAD, PDA, RCX, LCX and OM) which might be due to homogenous histology, anatomy and physiology of different coronary arteries. Consequently, biochemical variables cannot be used to locate the site of atherosclerosis in different arteries.

Our study had some limitations. For example, the number of subjects (sample size) was low, and it could be responsible for significant failure in the association between variables. We could not include all of the variables that affect atherosclerotic plaque, and this may be another limitation of this study. Therefore, it is recommended that conducting a study on a larger population and more effecting factors will be able to cover the gaps that became apparent in this study.

Conclusion:

We concluded that site of atherosclerotic plaque in different coronary arteries does not have any significant association with gender, age,

calcification and biochemical variables including FBS, TG, TC, HDL, and LDL which might be due

to same histological structure of different coronary arteries.

Table 4. The distribution and association of coronary artery sclerosis with laboratory values including FBS, LDL, HDL, Cholesterol and, Triglyceride

| | RCX | LCX | PDA | RCA | OM | LAD | FBS | P-value | LDL | P-value | HDL | P-value | Cholesterol | P-value | Triglyceride | P-value |
|--|----------|----------|----------|------------|----------|------------|--------|---------|------------|----------|-------|---------|-------------|---------|--------------|---------|
| | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (1.3%) | 0 (0.0%) | 2 (1.3%) | >70 | 0.692 | <130 | 0.835 | <25 | 0.022 | 200-240 | 0.612 | 200-240 | 0.327 |
| | 1 (0.7%) | 1 (0.7%) | 1 (0.7%) | 32 (21.2%) | 0 (0.0%) | 28 (18.5%) | 70-115 | 0.735 | 55 (36.4%) | 0.405 | 25-34 | 0.087 | >240 | 0.859 | >240 | 0.873 |
| | 0 (0.0%) | 2 (1.3%) | 1 (0.7%) | 48 (31.8%) | 1 (0.7%) | 32 (21.2%) | <115 | 0.952 | 8 (5.3%) | 0.857 | >34 | 0.135 | | 0.737 | | |
| | 0.495 | 0.905 | 0.952 | 0.735 | 0.669 | 0.692 | | | 70 (46.6%) | 0.007 | | | | | | |
| | 1 (0.7%) | 3 (2.0%) | 2 (1.3%) | 70 (46.6%) | 0 (0.0%) | 55 (36.4%) | | | 8 (5.3%) | 0.007 | | | | | | |
| | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 8 (5.3%) | 1 (0.7%) | 5 (3.3%) | | | 4 (2.6%) | 0.007 | | | | | | |
| | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 4 (2.6%) | 0 (0.0%) | 2 (1.3%) | | | 0.792 | 0.857 | | | | | | |
| | 0.926 | 0.792 | 0.857 | 0.797 | 0.007 | 0.835 | | | 0 (0.05) | 1 (0.7%) | | | | | | |
| | 0 (0.0%) | 0 (0.0%) | 1 (0.7%) | 10 (6.6%) | 0 (0.0%) | 4 (2.6%) | | | 0 (0.0%) | 0.007 | | | | | | |
| | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 23 (15.2%) | 1 (0.7%) | 30 (19.9%) | | | 0 (0.0%) | 0.007 | | | | | | |
| | 1 (0.7%) | 3 (2.0%) | 1 (0.7%) | 49 (32.5%) | 0 (0.0%) | 28 (18.5%) | | | 3 (2.0%) | 0.007 | | | | | | |
| | 0.655 | 0.276 | 0.135 | 0.087 | 0.405 | 0.022 | | | 0.655 | 0.276 | | | | | | |
| | 1 (0.7%) | 2 (1.3%) | 2 (1.3%) | 60 (39.7%) | 1 (0.7%) | 50 (33.1%) | | | 1 (0.7%) | 1 (0.7%) | | | | | | |
| | 0 (0.0%) | 1 (0.7%) | 0 (0.0%) | 17 (11.3%) | 0 (0.0%) | 10 (6.6%) | | | 0 (0.0%) | 0.007 | | | | | | |
| | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 5 (3.3%) | 0 (0.0%) | 2 (1.3%) | | | 0 (0.0%) | 0.007 | | | | | | |
| | 0.859 | 0.762 | 0.737 | 0.449 | 0.859 | 0.612 | | | 0.859 | 0.762 | | | | | | |
| | 1 (0.7%) | 3 (2.0%) | 2 (1.3%) | 63 (41.7%) | 1 (0.7%) | 49 (32.5%) | | | 1 (0.7%) | 1 (0.7%) | | | | | | |
| | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 18 (11.9%) | 0 (0.0%) | 10 (6.6%) | | | 0 (0.0%) | 0.007 | | | | | | |
| | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (0.7%) | 0 (0.0%) | 3 (2.0%) | | | 0 (0.0%) | 0.007 | | | | | | |
| | 0.873 | 0.663 | 0.761 | 0.273 | 0.873 | 0.327 | | | 0.873 | 0.663 | | | | | | |

Refereces:

1. Saadat S, Yousefifard M, Asady H, Moghadas Jafari A, Fayaz M, Hosseini M. The Most Important Causes of Death in Iranian Population; a Retrospective Cohort Study. *Emerg (Tehran)*. 2015;3(1):16-21.
2. Mack M, Gopal A. Epidemiology, traditional and novel risk factors in coronary artery disease. *Heart failure clinics*. 2016;12(1):1-10.
3. Munnur RK, Cameron JD, Ko BS, Meredith IT, Wong DT. Cardiac CT: atherosclerosis to acute coronary syndrome. *Cardiovascular diagnosis and therapy*. 2014;4(6):430.
4. Patel J, Al Rifai M, Blaha MJ, Budoff MJ, Post WS, Polak JF, et al. Coronary Artery Calcium Improves Risk Assessment in Adults With a Family History of Premature Coronary Heart Disease. *CLINICAL PERSPECTIVE: Results From Multiethnic Study of Atherosclerosis*. *Circulation: Cardiovascular Imaging*. 2015;8(6):e003186.
5. M R, SR N, H S, S RS, A A. The sonographic findings of subclinical atherosclerosis in common carotid arteries: Rheumatoid arthritis patients Versus control group. *Tehran University Medical Journal*. 2010;68(6):330-4.
6. Kazemiyan M, Afrasiab H, Pashaei MH. Comparison of the plaque rupture risk in different double-stenosis arrangements of coronary arteries by modeling fluid-structure interaction. *Modares Mechanical Engineering*. 2016;16(2):10-8.
7. Shikada T, Washio M, Nishizaki A, Kakino T, Ooe K, Ishibashi Y, et al. Risk factors for coronary artery calcification in Japanese patients. *Journal of cardiology*. 2015;66(1):36-40.
8. Madhavan MV, Gersh BJ, Alexander KP, Granger CB, Stone GW. Coronary artery disease in patients ≥ 80 years of age. *Journal of the American College of Cardiology*. 2018;71(18):2015-40.
9. Brainin P, Frestad D, Prescott E. The prognostic value of coronary endothelial and microvascular dysfunction in subjects with normal or non-obstructive coronary artery disease: A systematic review and meta-analysis. *International journal of cardiology*. 2018;254:1-9.
10. Ghafarzadegan R, Noruzi M, Mousavi M, Alizadeh Z, Harorani M, Javaheri J. The Effect of a Combined Herbal Ointment (Pepper, Rosemary, Peppermint) on Low back Pain after Coronary Angiography. *Journal of Medicinal Plants*. 2018;4(64):76-82.
11. Costantino S, Paneni F, Cosentino F. Ageing, metabolism and cardiovascular disease. *J Physiol*. 2016;594(8):2061-73.
12. Heidenreich PA, Trogon JG, Khavjou

- OA, Butler J, Dracup K, Ezekowitz MD, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation*. 2011;123(8):933-44.
13. Khoury Z, Schwartz R, Gottlieb S, Chenzbraun A, Stern S, Keren A. Relation of Coronary Artery Disease to Atherosclerotic Disease in the Aorta, Carotid, and Femoral Arteries Evaluated by Ultrasound. *The American Journal of Cardiology*. 1997;80(11):1429-33.
14. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. *Journal of the American College of Cardiology*. 2017;70(1):1-25.
15. Hajar R. Risk Factors for Coronary Artery Disease: Historical Perspectives. *Heart Views*. 2017;18(3):109-14.
16. Nakao YM, Miyamoto Y, Higashi M, Noguchi T, Ohishi M, Kubota I, et al. Sex differences in impact of coronary artery calcification to predict coronary artery disease. *Heart*. 2018;104(13):1118-24.
17. Mathur P, Ostadal B, Romeo F, Mehta JL. Gender-Related Differences in Atherosclerosis. *Cardiovasc Drugs Ther*. 2015;29(4):319-27.
18. Mathur P, Ostadal B, Romeo F, Mehta JL. Gender-Related Differences in Atherosclerosis. *Cardiovascular Drugs and Therapy*. 2015;29(4):319-27.
19. de Aloysio D, Gambacciani M, Meschia M, Pansini F, Modena AB, Bolis PF, et al. The effect of menopause on blood lipid and lipoprotein levels. *Atherosclerosis*. 1999;147(1):147-53.
20. Kardys I, Vliegenthart R, Oudkerk M. The female advantage in cardiovascular disease: Do vascular beds contribute equally? *Journal of Vascular Surgery*. 2008;47(2):479-80.
21. Ann SH, De Jin C, Singh GB, Lim KH, Chung J-W, Garg S, et al. Gender differences in plaque characteristics of culprit lesions in patients with ST elevation myocardial infarction. *Heart and vessels*. 2016;31(11):1767-75.
22. Rutsch F, Nitschke Y, Terkeltaub R. Genetics in arterial calcification: pieces of a puzzle and cogs in a wheel. *Circulation research*. 2011;109(5):578-92.
23. Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary Calcification, Coronary Disease Risk Factors, C-Reactive Protein, and Atherosclerotic Cardiovascular Disease Events. *The St Francis Heart Study*. 2005;46(1):158-65.
24. Frink RJ, Achor RWP, Brown AL, Kincaid

OW, Brandenburg RO. Significance of calcification of the coronary arteries. *The American Journal of Cardiology*. 1970;26(3):241-7.

25. Ohayon J, Finet G, Le Floc'h S, Cloutier G, Gharib AM, Heroux J, et al. Biomechanics of atherosclerotic coronary plaque: site, stability and in vivo elasticity modeling. *Ann Biomed Eng*. 2014;42(2):269-79.

26. O'Donnell CJ, Elosua R. [Cardiovascular risk factors. Insights from Framingham Heart Study]. *Rev Esp Cardiol*. 2008;61(3):299-310.

27. Reiner Ž. Hypertriglyceridaemia and risk of coronary artery disease. *Nature reviews Cardiology*. 2017;14(7):401.

28. Ahmed HM, Miller M, Nasir K, McEvoy JW, Herrington D, Blumenthal RS, et al. Primary Low Level of High-Density Lipoprotein Cholesterol and Risks of Coronary Heart Disease, Cardiovascular Disease, and Death: Results From the Multi-Ethnic Study of Atherosclerosis. *American Journal of Epidemiology*. 2016;183(10):875-83.