Journal of Society Medicine
Research & Review Articles on Diseases
*Journal of Society Medicine. 2025; 4 (3)*

# The Relationship Between Low-Density Lipoprotein Cholesterol and Coronary Artery Calcium Score in Patients with Chronic Coronary Syndrome Without Diabetes Mellitus at RSUP Haji Adam Malik Medan

Suci Asriri Pradina Muslim [1*], Hilfan Ade Putra Lubis [2], Ali Nafiah Nasution [2]

[1] *Resident of Cardiology Department, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*
[2] *Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*

***Corresponding Author**: Suci Asriri Pradina Muslim, Email: drsuciasriri@gmail.com

**ARTICLE INFO**

*Article history:*
Received
28 August 2024

Revised
11 Januari 2025

Accepted
31 March 2025

Manuscript ID:
JSOCMED-28012025-43-2

Checked for Plagiarism: Yes

Language Editor: Rebecca

Editor-Chief:
Prof. AznanLelo, PhD

**ABSTRACT**

**Introduction**: Chronic Coronary Syndrome (CCS) is the most common symptom of ischemic heart disease and is a major cause of morbidity and mortality worldwide. One of the associated risk factors for coronary heart disease events is Low Density Lipoprotein Cholesterol (LDL-C) through the process of atherosclerosis. Computed Tomography Coronary Artery (CTCA) is an examination that can be performed to assess atherosclerotic plaques and Coronary Artery Calcium Score (CAC Score). This study was conducted to assess the relationship between LDL and CAC Score in CCS patients.
**Methods**: This study is an observational analytical study involving 300 patients diagnosed with CCS during the period from March 1, 2023, to March 31, 2024, at RSUP H. Adam Malik Medan. All involved patients underwent LDL examination and CTCA examination as well as CAC Score measurement. Patient characteristics, disease history, and risk factors were also recorded.
**Results**: There was a significant relationship between LDL levels and CAC Score (P value: 0.008; OR: 1.91 (CI: 1.184-3.1). Among the patient characteristics in this study, the strongest protective factor was female gender (P value: <0.01; OR: 0.228 (CI: 0.119-0.437)), and the strongest risk factor was patients with hypertension (P value: 0.017; OR: 1.97 (CI: 1.119-3.484).
**Conclusion**: LDL can increase CAC Score in CCS patients.

**Keywords**

Chronic Coronary Syndrome, Low Density Lipoprotein Cholesterol, Computed Tomography Coronary Artery, Coronary Artery Calcium Score

***How to cite***: Muslim SAP, Lubis HAP, Nasution AN. The Relationship Between Low-Density Lipoprotein Cholesterol and Coronary Artery Calcium Score in Patients with Chronic Coronary Syndrome Without Diabetes Mellitus at RSUP Haji Adam Malik Medan. *Journal of Society Medicine*. 2025;4(3):76-83. **DOI: https://doi.org/10.71197/jsocmed.v4i3.203**

## INTRODUCTION

Chronic Coronary Syndrome (CCS) is the most common manifestation of ischemic heart disease and remains a leading cause of morbidity and mortality worldwide. In the United States, approximately 9 million patients suffer from angina [1]. Data from the 2013 and 2018 Indonesian National Health Surveys (Riskesdas) indicate that the prevalence of coronary heart disease (CHD) has remained at 1.5% per thousand individuals, with a notable increase from 0.5% in 2013 to 1.5% in 2018 [2]. Timely recognition and management of stable angina are crucial for reducing the risk of myocardial infarction. In addition to symptom recognition, risk stratification plays a vital role in patient management. Low-Density Lipoprotein Cholesterol (LDL-C) is a modifiable risk factor associated with coronary artery disease (CAD).

LDL-C contributes to atherosclerosis by accumulating in the intima of the arteries [3]. LDL-C is considered a primary modifiable risk factor for ischemic cardiovascular diseases and the main target of secondary cardiovascular prevention therapies. A reduction in LDL-C by just 1 mmol/L over five years can

reduce the incidence of major cardiovascular events by more than 20%. Epidemiological and genetic evidence suggests that LDL-C is a causative factor in cardiovascular disease, and several large-scale randomized controlled trials (RCTs) have shown that lowering LDL-C levels significantly reduces the risk of atherosclerosis and cardiovascular events [3].

Atherosclerotic plaques can be assessed using Computed Tomography Coronary Angiography (CTCA), a technique that detects atherosclerotic disease. CTCA can also indicate the risk of future cardiovascular events based on the severity of stenosis and the number of coronary vessels involved. In addition to the quantitative assessment of plaque severity, CTCA allows for the qualitative evaluation of plaques that indicate a high risk, including low attenuation and/or calcification [4]. CTCA is recommended as an initial diagnostic test for coronary artery disease in symptomatic patients where obstructive CAD cannot be excluded based on clinical evaluation alone. The relationship between CTCA findings and the coronary artery calcium (CAC) score as a predictor of coronary events is still under investigation. A post hoc analysis, such as the PREDICT study, demonstrated that coronary plaque imaging independently predicts coronary events in patients with suspected CAD and a low CAC Score [4].

According to the 2018 AHA/ACC cholesterol guidelines, the CAC Score is recommended as a third-step option after the 10-year cohort risk assessment for estimating risk and evaluating factors that may elevate the risk, particularly in discussions between physicians and patients. A CAC Score cutoff of 400 has been used in many studies to detect significant CAD or predict cardiovascular events. Other studies have shown that the frequency of significant ischemia, potential CAD, and cardiovascular events increases in patients with mild-to-moderate CAC Scores. Moreover, Shurong et al. demonstrated that the incidence of coronary artery disease was lowest in patients with a CAC Score of 0 and increased progressively with higher CAC Scores [5].

Cox regression analysis, adjusted for clinical characteristics, also indicated that a high CAC Score negatively impacted the long-term survival of patients with CCS. Shah et al. found that the extent of CAC serves as an independent estimator of long-term prognosis in symptomatic patients with luminal stenosis, helping guide prevention strategies for those without obstructive CAD [6]. Previous studies have examined the relationship between individuals with risk factors (e.g., family history of premature atherosclerotic heart disease, metabolic syndrome, chronic kidney disease, lipid parameters, and hsCRP) and the CAC Score in relation to the incidence of coronary heart disease. These studies found that the 10-year event rate was low in individuals with a CAC Score of 0. Furthermore, Martin et al. demonstrated that CCTA results can be used for risk stratification in patients with high LDL-C levels. A CAC Score of 0 is associated with a low incidence of atherosclerotic cardiovascular disease and mortality [7].

Given these insights, the present study aimed to explore the relationship between Low-Density Lipoprotein Cholesterol (LDL-C) and coronary artery calcium (CAC) score in patients with Chronic Coronary Syndrome (CCS).

## METHODS

This study employed an observational analytical design with a retrospective cohort approach, utilizing a comparative categorical unpaired analysis. The data collected included low-density lipoprotein cholesterol (LDL-C) levels and coronary artery calcium (CAC) scores obtained from Computed Tomography Coronary Angiography (CTCA) in patients diagnosed with Chronic Coronary Syndrome (CCS) at RSUP Haji Adam Malik Medan.

The research was conducted between March 2023 and March 2024, focusing on patients attending outpatient clinics at RSUP Haji Adam Malik Medan who underwent CTCA. This study primarily used secondary data extracted from the hospital's medical records. The target population consisted of all patients with CCS who underwent both LDL-C testing and CTCA at our institution. A consecutive sampling technique was used to select participants who met the inclusion and exclusion criteria.

The sample size was determined using a comparative unpaired categorical analysis formula. Based on the calculations, the minimum sample size required for each group was 99 participants, leading to a total of 198 participants in the study.

The study included patients who were diagnosed with CCS by a cardiologist at RSUP Haji Adam Malik and had LDL-C levels measured within three months before undergoing CTCA. The exclusion criteria were incomplete medical records, the presence of devices making CTCA unreadable, and diabetes mellitus.

Before the study began, ethical clearance was obtained from the Ethics Committee of the Faculty of Medicine at Universitas Sumatera Utara. All participants in this study were patients diagnosed with CCS who attended RSUP Haji Adam Malik Medan and who met the inclusion and exclusion criteria. CCS diagnosis was made according to the European Society of Cardiology (ESC) guidelines. Sampling was carried out using a quota (consecutive) method, with every eligible subject included until the required sample size of 21 patients per group was reached. The researcher reviewed the patients' medical records, including their medical history, physical examination, electrocardiogram (ECG), laboratory results, and CTCA data. Data for patients admitted before the study period were obtained from their medical records, whereas data for patients admitted during the study period were observed during their care. ECG was performed using a Bionet Cardiotouch 3000 machine at a speed of 25 mm/s and an amplitude of 10 mV, and a 12-lead ECG was recorded during the patient's first follow-up visit at the clinic.

CTCA was conducted using the Philips MSCT 128 slices machine, following the clinical judgment of the attending physician. After performing the CTCA, the CAC score was calculated and correlated with the results of the study. CAC score evaluation was performed by reviewing the CTCA images interpreted by a consultant cardiologist specializing in imaging. After data collection, the data were processed, analyzed, and hypothesis testing was performed using the SPSS version 25. Descriptive and bivariate statistical analyses were conducted, and multivariate analysis was performed to assess the most significant variables related to CAC and LDL-C. Statistical significance was set at a p-value of less than 0.05.

## RESULTS

This study was conducted on patients diagnosed with Chronic Coronary Syndrome (CCS) who underwent Computed Tomography Coronary Angiography (CTCA) at RSUP Haji Adam Malik Medan from March 2023 until the required sample size was achieved. A total of 300 patients met the inclusion and exclusion criteria.

Table 1. Baseline Characteristics of Study Subjects

| Parameter | Value |
|---|---|
| Age (years) | |
| ≥ 55 years | 137 (45.7%) |
| < 55 years | 163 (54.3%) |
| Gender | |
| Male | 119 (39.7%) |
| Female | 181 (60.3%) |
| Hypertension | |
| Present | 157 (52.3%) |
| Absent | 143 (47.7%) |
| CACS (score) | 248.03 (0-988) |
| CACS 0 | 107 (35.7%) |
| CACS ≥ 1 | 193 (64.3%) |
| LDL (mg/dL) | 113.08 (41-210) |
| LDL < 100 | 121 (40.3%) |
| LDL ≥ 100 | 179 (60%) |
| Statin | |
| Regular use | 142 (47.3%) |
| Not regular use | 158 (52.7%) |
| Smoking | |
| Smoker | 185 (61.7%) |
| Non-smoker | 115 (38.3%) |

The study sample comprised 300 patients. The majority of patients with CCS in this study were female, accounting for 60.3% of the population. Regarding age, 54.3% of the patients were younger than 55 years, and 45.7% were aged 55 years or older. Of the total study sample, 52.3% had hypertension and 47.7% did not. The

average Coronary Artery Calcium Score (CACS) for the entire sample was 248.03, and the mean LDL-C level was 113.08 mg/dL. In terms of statin use, 47.3% of the patients were on statins, whereas 52.7% were not. Furthermore, 61.7% of the patients were smokers, whereas 38.3% had never smoked. The characteristics are summarized in Table 1.

Table 2. Association Between Baseline Characteristics and CACS

| Variable | CACS ≥ 1 (n, %) | CACS 0 (n, %) | p-value |
|---|---|---|---|
| Gender | | | 0.02* |
| Female | 107 (55.4%) | 74 (69.2%) | |
| Male | 86 (44.6%) | 33 (30.8%) | |
| Hypertension | | | 0.002* |
| Present | 114 (59.1%) | 43 (40.2%) | |
| Absent | 79 (40.9%) | 64 (59.8%) | |
| Age ≥ 55 years | | | <0.001** |
| ≥ 55 years | 113 (58.5%) | 24 (22.4%) | |
| < 55 years | 80 (41.5%) | 83 (77.6%) | |
| Statin Use | | | 0.001* |
| Not Regular Statin | 78 (40.4%) | 64 (59.8%) | |
| Regular Statin | 115 (59.6%) | 43 (40.2%) | |
| Smoking | | | 0.048* |
| Smoker | 127 (65.8%) | 58 (54.2%) | |
| Non-Smoker | 66 (34.2%) | 49 (45.8%) | |
| LDL | | | 0.008* |
| LDL ≥ 100 | 126 (65.3%) | 53 (49.5%) | |
| LDL < 100 | 67 (34.7%) | 54 (50.5%) | |

Noted: *, Chi-square test; **, T-test for unpaired data

Table 3. Multivariate Analysis of Variables Affecting CACS

| Variable | Adjusted OR | CI 95% | p-value |
|---|---|---|---|
| Female Gender | 0.228 | 0.119 – 0.437 | < 0.01 |
| Age ≥ 55 years | 1.110 | 1.076 – 1.145 | < 0.01 |
| Hypertension | 1.974 | 1.119 – 3.484 | 0.017 |
| LDL ≥ 100 | 1.012 | 1.004 – 1.020 | 0.004 |
| Statin Use | 0.410 | 0.233 – 0.724 | 0.002 |

Noted: *, Logistic Regression

To assess the relationship between baseline characteristics (such as sex, hypertension, age, statin use, and smoking) and CAC score, a chi-square test was performed, and the degree of association was determined using Odds Ratios (OR). The analysis found a significant negative association between sex and CACS ($p = 0.02$). The percentage of women with a CACS of 0 was higher than that of men (69.2 %). Hypertension was significantly positively associated with CAC Score ($p = 0.002$), with hypertensive patients having a higher proportion of CACS ≥ 1 (59.1%) than non-hypertensive patients. Age showed a significant positive relationship with CACS ($p < 0.001$), with patients aged ≥ 55 years having a higher proportion of CACS ≥ 1 (58.5%) than those aged < 55 years.

The analysis also revealed significant associations between statin use, smoking, and CACS. Statin use was significantly negatively associated with CACS, with 40.4% of patients who used statins having CACS ≥ 1, compared to 59.6% in those who did not use statins. Smoking was positively associated with an increased CACS, as 65.8% of smokers had CACS ≥ 1, compared to 54.2% of non-smokers. Additionally, a Chi-square test revealed a significant positive relationship between LDL levels and CAC score ($p = 0.008$), with patients with LDL ≥ 100 mg/dL having a higher incidence of CACS ≥ 1 than those with LDL < 100 mg/dL. This is presented in Table 2.

Multivariate logistic regression analysis was performed to identify the most influential factors and assess the strength of the associations. The results indicated that sex (female) was the strongest protective factor, with an odds ratio (OR) of 0.228. Statin use was also a protective factor, with an OR of 0.410. Conversely, age, hypertension, and high LDL levels were identified as risk factors. Hypertension showed the highest risk of increasing the CAC score, with an OR of 1.974. Age ≥ 55 years had an OR of 1.110, and LDL levels ≥ 100 mg/dL had an OR of 1.012. These findings are summarized in Table 3.

## DISCUSSION

This study investigated the association between Low-Density Lipoprotein Cholesterol (LDL-C) levels and Coronary Artery Calcium (CAC) score in patients with Chronic Coronary Syndrome (CCS) without Diabetes Mellitus. While previous studies, such as those conducted by Shi et al. in 2020, focused on populations with Diabetes Mellitus, this study provides new insights into patients without diabetes by analyzing the direct relationship between LDL and CAC scores.

The CAC score is an emerging method for predicting the severity of coronary artery stenosis and cardiovascular events. It serves as a valuable prognostic tool for cardiovascular diseases, as demonstrated in many studies. One critical factor influencing the formation and stability of coronary plaques is the LDL-C level. This study confirmed a positive association between LDL-C levels and CAC scores, where patients with LDL ≥ 100 mg/dL exhibited a higher proportion of CAC ≥ 1 (65.3%) than those with LDL < 100 mg/dL. These findings align with those of Miname et al., who also observed a significant correlation between higher LDL-C levels and elevated CAC scores [8].

Arterial wall calcification is driven by various factors, including the differentiation of osteoblast-like cells and lipid accumulation in the subendothelial space, which may induce calcification. Oxidized lipids play crucial roles in this process [9]. The findings of this study suggest that higher LDL-C levels contribute to increased coronary calcification, which supports the growing body of evidence linking LDL-C with CAC score progression.

Another significant finding of this study was the relationship between sex and CAC scores. In line with the previous research by Makaryus et al., which found that men generally have higher CAC scores than women, our study also indicated that females had a higher percentage of CAC 0 (69.2%) than males (30.8%) [10,11]. This could be attributed to hormonal differences, as premenopausal women are protected by estrogen, which has anti-atherosclerotic effects and reduces the risk of coronary artery disease. Estrogen decreases atherosclerotic plaque burden and regulates inflammatory processes in the arterial walls, which may explain the lower prevalence of high CAC scores in females [12]. However, Achenbach (2018) suggested that CAC ≥ 1 has a greater impact on cardiovascular mortality in women than in men, highlighting the need for further investigation into sex differences in coronary calcification [13].

Hypertension was a significant factor associated with increased CAC scores. The study found that 59.1% of hypertensive patients had CAC ≥ 1, compared to 40.9% of non-hypertensive patients. This finding aligns with studies by Jeonggu et al. (2019) and Wang et al., which indicated that hypertension is strongly linked to higher CAC scores and accelerated plaque formation [14-16]. Hypertension induces endothelial damage by increasing pressure on the arterial walls, promoting plaque formation and progression. Xinhua et al. (2020) also demonstrated that elevated blood pressure correlates with increased coronary calcium deposition, further supporting the pathogenic role of hypertension in coronary artery disease [17].

This study also explored the relationship between statin use and CAC scores. Statins are widely recommended as the primary therapy to reduce lipid levels and are used in both primary and secondary prevention of coronary artery disease. In this study, patients who did not regularly use statins had a higher prevalence of CAC ≥ 1 (59.6%) than those who used statins regularly. This finding is consistent with the guidelines suggesting that statins reduce lipid accumulation in coronary plaques, potentially stabilizing vulnerable plaques. However, Shahraki et al. (2023) found in their systematic review that while statins might slow CAC progression, their effect on reducing the CAC score remains inconclusive across different populations [18].

While statins have been shown to reduce the risk of coronary ischemic events by stabilizing plaques, studies such as those conducted by Lai et al. have found that statin therapy in high-risk individuals did not significantly alter CAC progression [19]. Furthermore, Mitchell et al. found that statins may offer long-term benefits in reducing the risk of cardiovascular events in patients with higher CAC scores, particularly those with a CAC score > 100 [20]. However, the relationship between statin use and CAC score progression remains complex and warrants further research, especially in populations without cardiovascular disease symptoms.

Smoking was another significant factor identified in this study, with 65.3% of smokers having CAC ≥ 1. This is consistent with the findings of Hirooka et al. (2013) and Marcus et al. (2015), who showed that smoking, particularly with a higher pack-year history, was strongly associated with increased CAC scores [17-19]. Smoking induces atherosclerosis and accelerates plaque formation through various mechanisms, including oxidative stress and inflammation of the vascular walls. Petsophonsakul et al. (2020) demonstrated that nicotine promotes a pro-calcification process via the activation of Nox5, leading to increased vascular calcification [21-24].

In conclusion, this study provides valuable insights into the relationship between LDL-C and CAC scores in patients with Chronic Coronary Syndrome without Diabetes Mellitus. These findings support the existing literature that higher LDL-C levels are associated with increased coronary artery calcification. Sex, hypertension, statin use, and smoking were also identified as significant factors influencing CAC scores. Future studies should focus on longitudinal data to better understand the long-term effects of statin therapy, smoking cessation, and blood pressure management on CAC progression and the cardiovascular outcomes.

## CONCLUSION

This study established a positive relationship between LDL-C levels and CAC score in patients with Chronic Coronary Syndrome (CCS), highlighting the significant role of LDL in the progression of coronary artery calcification. The findings also suggest that sex, with females showing a protective effect, and hypertension, as a major risk factor, have a substantial impact on CAC score outcomes. These results underscore the importance of managing LDL-C levels and hypertension in patients with CCS while also considering sex differences in risk assessment and prevention strategies. Further research is needed to explore these associations in greater depth and evaluate the long-term effects of the interventions on coronary calcification and cardiovascular events.

## DECLARATIONS

None

## CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

## FUNDING

None

## COMPETING INTERESTS

The authors declare no conflicts of interest in this review.

## AUTHORS' CONTRIBUTIONS

All authors contributed to the work, including data analysis, drafting, and reviewing. They approved the final version and are accountable for all aspects of the study.

## ACKNOWLEDGMENTS

None

## REFERENCE


1. Hermiz C, Yub Raj S. Angina. Natl Libr Med. 2022; 19:12.
2. Riskesdas. Hasil utama Riset Kesehatan Dasar. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018.
3. Shi R, Gao Y, Shen LL, Shi K, Wang J. The effect of LDL-C status on the association between increased coronary artery calcium score and compositional plaque volume progression in statins-treated diabetic patients: evaluated using serial coronary CTAs. Cardiovasc Diabetol. 2022; 21:121.
4. Yamamoto H, Kihara Y, Fujimoto S, Daida H. Predictive value of the coronary artery calcium score and advanced plaque characteristics: Post hoc analysis of the PREDICT registry. J Cardiovasc Comput Tomogr. 2021;15(2):148-53.
5. Zheng P, Zeng B, Zhou C, Liu M. Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism. Mol Psychiatry. 2016;21(6):786-96.
6. Zahr FE, Mulukutla SR, Marroquin OS. A contemporary overview of the pathophysiology of angina pectoris. Rev Cardiovasc Med. 2013;14(1):3-10.
7. Tarkin JM, Kaski JC. Pharmacological treatment of chronic stable angina pectoris. Clin Med. 2013;13(1):63-70.
8. Miname MH, Bittencourt MS, Moraes SR, Alves RIM. Coronary artery calcium and cardiovascular events in patients with familial hypercholesterolemia receiving standard lipid-lowering therapy. JACC Cardiovasc Imaging. 2019;12(9):1797-805.
9. Kozakova M, Morizzo C, Jamagidze G, Latta DD. Association between low density lipoprotein cholesterol and vascular biomarkers in primary prevention. Biomedicines. 2023; 11:1753.
10. Sandesara PB, Anurag M, Wesley T, Heval M. Clinical significance of zero coronary artery calcium in individuals with LDL cholesterol ≥ 190 mg/dL: the multi ethnic study of atherosclerosis. J Atheroscler. 2019.
11. Makaryus AN, Sison C, Kohansieh M, Makaryus JN. Implications of gender difference in coronary calcifications as assessed by CT coronary angiography. Clin Med Insights Cardiol. 2019;8(4).
12. Lennep JE, Tokgozoglu LS, Badimon L, Dumanski S. Women, lipids, and atherosclerotic cardiovascular disease: a call to action from the European Atherosclerotic Society. Eur Heart J. 2023; 44:4157-73.
13. Achencbach S. Coronary calcium bad news for men, even worse for women. Eur Heart J. 2018; 39:3736-8.
14. Reddy SM, Rubenfire M, Jackson L, Brook R. Coronary artery calcium in hypertension. J Am Soc Hypertens. 2019;9(12):993-1000.
15. Sung KC, Lee MY, Kim JY, Park JB. Prediction of incident hypertension with the coronary artery calcium score based on the 2017 ACC/AHA high blood pressure guidelines. Hypertens Res. 2020; 43:1293-300.
16. Won KB, Han D, Choi SY, Chun EJ. Association between blood pressure classification defined by the 2017 ACC/AHA guidelines and coronary artery calcification progression in an asymptomatic adult population. Eur Heart J. 2021; 1:1-9.
17. Xinhua W, Jian G, Krishnam MS, Robert D. Pulse pressure correlates with coronary artery calcification and risk for coronary heart disease. Coron Artery Dis. 2019;30(4):297-302.
18. Shahraki MN, Jouabadi SM, Bos D, Stricker B. Statin use and coronary artery calcification: a systematic review and meta-analysis of observational studies and randomized controlled trials. Curr Atheroscler Rep. 2023; 25:769-84.
19. Lai R, Ju J, Lin Q, Xu H. Coronary artery calcification under statin therapy and its effect on cardiovascular outcomes: a systematic review and meta-analysis. Front Cardiovasc Med. 2020;7.
20. Mitchell JD, Fergestrom N, Gage BF, Paisley R. Impact of statins on cardiovascular outcomes following coronary artery calcium scoring. J Am Coll Cardiol. 2018;72(5):3233-42.
21. Ngamdu KS, Ghosalkar DS, Chung HE, Christensen JL. Long-term statin therapy is associated with severe coronary artery calcification. PLoS One. 2023;18(7):1-13.

22. Marcus JS, Valenti V, Hartaigh B, Gransar H. Prognostic utility of coronary artery calcium scoring in active smokers: a 15-year follow-up study. Int J Cardiol. 2015;177(2):581-3.
23. Oshunbade A, Yimer W, Valle K, Hamid A. Cigarette smoking, incident of coronary heart disease, and coronary artery calcification in black adults: the Jackson Heart Study. J Am Heart Assoc. 2021.
24. Petsophonsakul P, Burgmaier M, Willems B, Heeneman S. Nicotine promotes vascular calcification via intracellular Ca2+-mediated, NOX5-induced oxidative stress and extracellular vesicle release in vascular smooth muscle cells. Eur Soc Cardiol. 2022;118(9):2196-210.