



Cardiometabolic phenotypes and imaging markers of coronary plaque instability: A multimodal analysis

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Abstract. The present study provides a comprehensive assessment of the association between cardiovascular imaging signatures of coronary atherosclerosis progression and the cardiometabolic phenotype, specifically focusing on metabolic and behavioral risk factors in patients with coronary artery disease (CAD). Using data obtained from multislice computed tomography coronary angiography (MSCT-CA), including the Agatston coronary artery calcium score, a correlation analysis was performed with dysmetabolic and behavioral cardiovascular risk factors such as obesity, dyslipidemia (LDL-C and HDL-C levels), arterial hypertension, smoking, physical inactivity, and psychoemotional stress depending on the clinical course of CAD.

The study demonstrated that the strength of the association between coronary artery calcium and cardiovascular risk factors was determined by the clinical phenotype of CAD. In stable CAD, the strongest correlations were observed with age, arterial hypertension, and dyslipidemia, whereas no significant differences were identified regarding the relationship between calcium score, smoking, and obesity between stable and unstable angina groups. Correlations between coronary calcium burden, physical inactivity, and psychological stress remained weak regardless of the clinical course of the disease.

These findings demonstrate the differentiated impact of cardiovascular risk factors on various aspects of atherosclerotic progression and may contribute to the development of more precise risk stratification strategies and individualized prognostic assessment in patients with CAD.

Keywords: Coronary artery disease; cardio-imaging; multislice computed tomography coronary angiography; coronary artery calcium score; cardiovascular risk factors; arterial hypertension; smoking; obesity; physical activity; dyslipidemia; psychological stress.

1. Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality globally, accounting for approximately 17.9 million deaths in 2019—nearly 32 % of all deaths—with over 75 % occurring in low- and mid-dle-income countries [1]. Coronary artery disease (CAD), is the most critical component of this burden, responsible for about 18.6 % of global mortality in 2019 [2]. Despite improve-ments in age-adjusted mortality from CAD, the absolute number of deaths attributed to CAD is growing, likely due to factors such as an aging global population and in-creased risk factor risk factors such as obesity, diabetes, and smoking, particularly in low- and middle-income countries [3], underscoring the urgent need for effective prevention and treatment strategies tailored to diverse socioeconomic contexts.

The pathogenesis of CAD is a complex multifactorial process involving genetic, epigenetic, inflammatory, and metabolic mechanisms leading to the formation and progression of atherosclerotic lesions within the coronary arteries [4]. Endothelial dysfunction, chronic inflammation, and lipid metabolism disorders play a crucial role in the development of atherosclerotic plaques with varying morphology and stability [5]. Modern research highlights the importance of integrating clinical, laboratory, and imaging biomarkers to assess the progression of coronary heart disease [11, 15].

Particular importance in CAD pathogenesis is attributed to coronary artery calcification, which is considered a dynamic and regulated process closely associated with traditional cardiovascular risk factors. Arterial hypertension, dyslipidemia, smoking, obesity, physical inactivity, and chronic psychoemotional stress exert a complex impact on the vascular wall, contributing not only to atherosclerotic progression but also to vascular calcification [6–9, 12, 13]. Microcalcifications are associated with inflammation, neovascularization, and plaque instability, thereby increasing the risk of plaque rupture and acute coronary syndromes, whereas macrocalcification reflects a more stable stage of the atherosclerotic process [14].

Multislice computed tomography coronary angiography (MSCT-CA) occupies a key position among noninvasive diagnostic modalities for CAD. In addition to anatomical visualization, this technique enables quantitative assessment of coronary artery calcification using the coronary artery calcium score (Agatston score), which reflects the total atherosclerotic burden and indirectly

characterizes plaque stability [10]. Modern studies confirm the high diagnostic and prognostic value of MSCT-AH in risk stratification in patients with coronary heart disease [15].

The present study aimed to perform a correlation analysis between MSCT-CA parameters, including coronary artery calcium score, and traditional cardiovascular risk factors in patients with CAD. Particular attention was paid to evaluating the contribution of these factors to coronary calcification and the progression of coronary atherosclerosis in different clinical forms of CAD, namely stable and unstable angina pectoris.

2. Materials and methods

A total of 152 patients of both sexes undergoing treatment at the Cardiology Department of the multidisciplinary clinic of Tashkent State Medical University were enrolled in the study. The mean age of participants was 60.9 ± 1.46 years. The main group consisted of 73 patients diagnosed with unstable angina, whereas the comparison group included 79 patients with stable exertional angina pectoris functional class III.

At baseline, no statistically significant differences were identified between the groups regarding age, sex, duration of CAD, or prevalence of comorbidities.

Cardiovascular risk factors were assessed using the following methods. Blood pressure was measured using an automated sphygmomanometer, and the average of three measurements was recorded. Smoking status was assessed using a standardized questionnaire with calculation of pack-years. Dyslipidemia was evaluated through biochemical analysis of fasting venous blood samples obtained after 12 hours of fasting, including total cholesterol, LDL-C, HDL-C, and triglyceride levels. Physical activity was assessed using the short form of the International Physical Activity Questionnaire (IPAQ). Psychoemotional stress levels were evaluated using the validated Reeder Stress Scale.

To assess cardio-imaging aspects of CAD progression, analysis of imaging biomarkers obtained by MSCT coronary angiography was performed. Examinations were carried out at the radiology department equipped with multidetector computed tomography at the Republican Specialized Scientific and Practical Center of Cardiology.

In the present study, coronary MSCT-CA was performed using a 64-slice CT scanner with ECG synchronization and breath-hold protocol to minimize motion artifacts. Slice thickness ranged from 0.75 to 2 mm, providing high spatial resolution for detailed visualization of coronary artery anatomy.

Before contrast administration, low-dose CT scanning was performed to evaluate coronary calcification. The acquired data were processed using specialized software allowing quantitative assessment of coronary artery calcium score according to the Agatston method. The calcium score served as a predictor of the extent of atherosclerotic involvement. Additionally, total atherosclerotic plaque burden was calculated as the sum of the volumes of all identified coronary plaques. Following contrast administration and ECG synchronization, coronary artery scanning was performed during the optimal phase of the cardiac cycle.

Statistical analysis was conducted using STATISTICA 6.0 and SAS 6.3 software packages. Electronic databases were created using Microsoft Excel Office 2020. Statistical significance was assessed using Wald's criterion, with $p < 0.05$ considered statistically significant. Spearman correlation analysis was applied.

3. Results and discussion

Correlation analysis between age and cardio-imaging patterns of coronary atherosclerosis demonstrated statistically significant differences between unstable and stable angina groups, confirming the role of age as a nonmodifiable yet cumulatively acting factor in CAD progression and determining its specific influence on plaque morphology in different clinical settings.

The strongest correlation was observed between age and coronary artery calcium score (Agatston score). In patients with stable angina, a pronounced positive correlation was identified ($r = 0.65$, $p < 0.001$), which is expected considering the gradual accumulation of calcium within atherosclerotic plaques over time. This finding reflects the chronic nature and prolonged progression of atherosclerosis in stable CAD. In contrast, in the unstable angina group, this relationship was moderate ($r = 0.40$, $p < 0.01$). This difference may be explained by the fact that acute coronary events are often associated with rupture of relatively "young," less calcified but highly vulnerable plaques, which may develop in younger patients or progress rapidly.

Correlation analysis between arterial hypertension and cardio-imaging patterns of coronary atherosclerosis revealed statistically significant differences between the study groups, confirming the differentiated pathogenetic influence of hypertension on various aspects of the atherosclerotic process.

In patients with stable angina, a pronounced positive correlation between arterial hypertension and coronary calcium score was observed ($r = 0.55$, $p < 0.001$), whereas in unstable angina this association was moderate ($r = 0.35$, $p < 0.01$). These findings are consistent with the established role of hypertension as a major contributor to arterial stiffness and vascular calcification. In stable CAD, characterized by a prolonged disease course, the cumulative effect of hypertension results in marked calcium deposition within atherosclerotic plaques.

Correlation analysis also revealed statistically significant and differentiated associations between smoking and cardio-imaging patterns of coronary atherosclerosis. Pathogenetically, smoking accelerates atherogenesis through endothelial dysfunction, oxidative stress, and systemic inflammation. In the stable angina group, a moderate positive correlation between smoking and coronary artery calcium score was identified ($r = 0.45$, $p < 0.01$), whereas in unstable angina the association was also moderate but weaker ($r = 0.32$, $p < 0.05$). These findings indicate that prolonged smoking contributes to calcium accumulation within coronary arteries, representing a marker of chronic and advanced atherosclerosis.

Subsequent analysis demonstrated significant associations between obesity and cardio-imaging biomarkers, reflecting its complex impact on plaque morphology and progression in patients with stable and unstable angina. Through chronic systemic inflammation, insulin resistance, dyslipidemia, and activation of the renin-angiotensin-aldosterone system, obesity acts as a major driver of atherogenesis. In both groups, moderate positive correlations between obesity and coronary calcium score were identified ($r = 0.40$ and $r = 0.45$ respectively; $p < 0.01$), indicating that obesity contributes to vascular calcium accumulation regardless of clinical presentation.

Despite the well-established role of physical inactivity in promoting atherogenesis through worsening dyslipidemia, insulin resistance, and systemic inflammation, direct correlations with quantitative MSCT-CA parameters were less pronounced. Weak negative correlations between physical inactivity and coronary calcium score were observed in both unstable and stable angina groups ($r = -0.20$ and $r = -0.28$ respectively; $p < 0.05$).

The study also identified significant correlations between dyslipidemia parameters, particularly LDL-C and HDL-C levels, and cardio-imaging patterns of coronary atherosclerosis progression. In the unstable angina group, moderate positive and negative correlations between LDL-C and HDL-C respectively and coronary calcium score were observed (LDL-C: $r=0.35$, $p<0.05$; HDL-C: $r=-0.40$, $p<0.05$). In stable angina, these associations were substantially stronger (LDL-C: $r=0.60$; HDL-C: $r=-0.62$; $p<0.01$), reflecting a more stable pattern of atherosclerotic progression associated with lipid profile disturbances.

Furthermore, statistically significant correlations between psychoemotional stress levels and coronary atherosclerosis progression patterns assessed by MSCT-CA were identified. In patients with unstable angina, stress level demonstrated weak positive correlations with coronary calcium score ($r=0.20$, $p<0.05$). Similar but less pronounced correlations were observed in stable angina patients ($r=0.30$, $p<0.05$). These findings support the pathogenetic hypothesis regarding the role of chronic stress in accelerating coronary atherosclerosis.

4. Conclusions

The performed correlation analysis identified clear differentiated relationships between nonmodifiable (age) and modifiable (arterial hypertension, smoking, obesity) cardiovascular risk factors and morphostructural characteristics of coronary atherosclerosis in patients with stable and unstable angina.

Age and arterial hypertension exert cumulative effects on atherosclerotic progression and are associated with increased calcification in stable CAD. In unstable angina, these factors are more closely associated with the formation of vulnerable, less calcified, lipid-rich plaques predisposing to acute coronary events.

Smoking and obesity additionally contribute to diffuse and multivessel coronary involvement, stimulate lipid core accumulation, and reduce plaque density, thereby increasing plaque instability, particularly in patients with unstable angina.

The obtained findings improve understanding of the pathogenetic mechanisms underlying the morphological dynamics of atherosclerotic plaques in different clinical scenarios of CAD. Thus, the study results emphasize the necessity of a personalized approach to CAD management considering the specific influence of cardiovascular risk factors on morphofunctional characteristics of coronary plaques.

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