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ORIGINAL ARTICLE

Comparison of coronary artery calcium scores between patients with and without type 2 diabetes

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ABSTRACT

Aim To compare the extent of coronary artery calcification in patients with and without type 2 diabetes mellitus (T2DM) using Coronary Computed Tomography Angiography (CCTA).

Methods This retrospective, observational cohort study included 107 patients who underwent CCTA at the Clinical Centre of the University of Sarajevo between July and December 2024. The patients were divided into two groups: those with T2DM (n=51) and those without T2DM (n=56). Laboratory parameters, demographic data, and calcium scores were analysed. The calcium score was categorised into six groups based on cardiovascular risk, and the comparison was made using appropriate statistical analysis.

Results Patients with T2DM had significantly higher calcium scores than non-diabetic patients (p=0.0001). In the T2DM group, 18 (35.3%) patients had a calcium score >400, indicating high cardiovascular risk. Patients without diabetes were more frequently classified into lower-risk categories (p=0.0001). A significant correlation was found between calcium score and age (r=0.442; p=0.001) and gender (r=-0.218; p=0.024), with males having a higher calcium score. A total cholesterol, LDL, and uric acid levels were significantly higher in diabetic patients (p=0.005, p=0.025, and p=0.03, respectively).

Conclusion This study confirms a strong association between T2DM and increased coronary artery calcification. Age and male gender are significant predictors of higher calcium scores. Further research is needed to explore these relationships, particularly within the Bosnian population.

Keywords: coronary angiography, coronary artery calcification, coronary disease, diabetes mellitus type 2

INTRODUCTION

The correlation between arterial calcifications and cardiovascular disease (CVD) is well-established and has been acknowledged by anatomists and pathologists for generations (1). Radiological detection of coronary artery calcification in vivo by fluoroscopy was first described in the late 1950s (2). Subsequently, the association between the presence of coronary artery calcification and an increased risk of cardiovascular events was also demonstrated (3). Coronary Computed Tomography Angiography (CCTA) is a non-invasive diagnostic method that employs computed tomography to assess the existence and severity of coronary artery calcification. It evaluates vessel morphology, stenoses, atherosclerotic plaques, and calcifications. The first scan, without contrast, quantifies coronary artery calcium (Agatston score) and detects calcified plaques. The second scan, with contrast, visualises the vessel lumen, identifying soft plaques and arterial narrowing, which is crucial for assessing patency and haemodynamic impact (4). The overall severity of calcification is considered to be a better indicator of the extent of coronary atherosclerosis than the severity of individual stenoses (5). The absence of coronary artery calcification, especially in asymptomatic patients, correlates with unremarkable coronary artery stenoses and indicates a low overall cardiovascular risk (6).

Coronary artery calcification is observed in most patients with myocardial ischaemia, with or without presenting symptoms (7). Asymptomatic myocardial ischaemia is the most common manifestation of coronary artery disease (CAD) and accounts for more than 75% of ischaemic episodes during routine daily activity. Most silent ischaemic episodes occur during minimal or no physical exertion (8). However, it is important to note that although coronary artery calcification is common, especially in older age and in males, the presence of calcification does not necessarily indicate the presence of ischaemic heart disease (9). Until recently, vascular calcification was considered an inevitable part of the ageing process, and the development of coronary artery calcification was considered a passive process (10). However, emerging studies have shown that calcification formation

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is an active pathophysiological process not solely attributable to age, revealing some major underlying mechanisms (11). Several conditions such as type 2 diabetes mellitus (T2DM) and metabolic disturbances have been identified as major predisposing factors. Hyperlipidaemia promotes vascular calcification. Low-density lipoprotein (LDL) oxidation contributes to the formation of pro-osteogenic mediators (12), and ectopic bone formation in atherosclerosis initiates coronary artery calcification (13). Oxidative stress, associated with several mediators, may represent a major link between inflammation and calcification. Atherosclerosis and vascular calcification are driven by a low-intensity inflammatory process, triggered by apolipoproteins and oxidised phospholipids within the arterial wall (14). Persistently high blood glucose levels promote coronary artery calcification by inducing the production of mediators that shift the phenotype of vascular smooth muscle cells toward osteoblast-like cells, making diabetic patients especially vulnerable. In some cases, insulin exerts an inhibitory effect, but this influence is contingent upon the severity of the metabolic disorder and the degree of insulin resistance (15).

A detailed analysis of the existing studies leads to the conclusion that diabetes causes accelerated coronary artery calcification through a variety of pathophysiologic processes. However, multiple studies have shown that, while T2DM is associated with the existence of calcified atherosclerosis, particularly in the coronary arteries, it does not always correspond with its severity. Further research is required to clarify these connections, and to the best of our knowledge, no such studies have been performed in Bosnia and Herzegovina.

This study aims to compare the extent of coronary artery calcification in patients with and without T2DM, using CT coronary angiography.

PATIENTS AND METHODS

Patients and study design

This retrospective, observational cohort study included 107 patients who underwent CCTA at the Clinic of Radiology, Clinical Centre of the University of Sarajevo, between 1 July and 31 December 2024. The patients were divided into two groups: patients with T2DM and patients without T2DM. The diagnosis of T2DM was made based on laboratory parameters: elevated blood glucose value (fasting blood glucose ≥7 mmol/L), glycosylated haemoglobin HbA1c (≥6.5%), and a history of taking diabetes medications (oral antidiabetic drugs, insulin, or both).

The inclusion criteria were patients aged 18 to 75 years with a complete medical history. Exclusion criteria were patients ≤18 or >75 years of age, incomplete and inadequate medical documentation, active oncological and haematological disease, end-stage chronic kidney disease, and severe electrolyte imbalance.

The study was approved by the Ethics Committee of the Clinical Centre of the University of Sarajevo.

Methods

Demographic and clinical data were collected through a detailed analysis of patients' medical records containing physical examination data, laboratory findings, and CCTA results. Venous blood samples were taken from each patient, and laboratory parameters were monitored: platelet count (PTL), mean platelet volume (MPV), total cholesterol, LDL, high-density lipoprotein (HDL), triglycerides, uric acid, serum calcium (Ca), and C-reactive protein (CRP).

Calcium score values were obtained from CCTA results performed on the Aquilion Prime CT scanner (Canon Medical Systems Corporation, Tochigi, Japan), using a lobitridol contrast agent. The calcium score was calculated using several parameters. The area of each calcification was measured in square millimetres and multiplied by the calcium density within the calcification. The individual results for all arterial segments were then summed to derive the total calcium score (16). Based on the total calcium score, patients were divided into six groups: I - Calcium score 0 (no calcifications in the coronary arteries, no risk of CAD); II - Calcium score 1-9 (very few calcifications, minimal risk for CAD); Group III - Calcium score 10-99 (mild calcifications, low risk for CAD); IV - Calcium score 100-399 (moderate calcifications, moderate risk for CAD); V - Calcium score >400 (significant calcifications, high risk for CAD), and Group VI - Calcium score >1000 (extensive calcifications, very high risk for CAD).

Statistical analysis

The results were presented in tables and graphically through the numbers, percentages, arithmetic mean (M) with standard deviation (SD), median and interquartile range (IQR), and range of values depending on the type of data. A comparison of the obtained results was performed using the $\chi 2$ test, Student's t-test, and Mann-Whitney test. Correlation analysis was performed using the non-parametric Spearman's coefficient. Test results were considered statistically significant at a confidence level of 95% ($p<0.05$).

RESULTS

A total of 107 patients were included in the study, predominantly females, 75 (70%). The patients were categorised into two groups: 51 with T2DM and 56 without T2DM. Both diabetic and non-diabetic groups consisted mainly of females, 29 (56.8%) and 29 (82.1%), respectively. The mean age in the non-diabetic group was 62.14±10.04 years, while in the T2DM group it was 66.04±9.68. Although the patients in the diabetic

Table 1. Representation of patients according to calcium score categories with percentages within the group

CACS group according to calcium score	No of patients in the Group		Total
	Without DM2	With DM2	
I - CACS 0 (without CAD)	15 (26.8)	4 (7.8)	19 (17.8%)
II - CACS 1-9 (minimal risk for CAD)	11 (19.6%)	6 (11.8%)	17 (15.9%)
III - CACS 10-99 (low risk for CAD)	18 (32.1%)	4(7.8%)	22 (20.6%)
IV - CACS 100-399 (moderate risk for CAD)	7 (12.5%)	19 (37.3%)	26 (24.3%)
V - CACS>400 (high risk for CAD)	4 (7.1%)	7 (13.7%)	11 (10.3%)
VI - CACS>1000 (very high risk for CAD)	1 (1.8%)	11 (21.6%)	12 (11.2%)
Total	56 (52.3%)	51 (47.7%)	107 (100%)

DM2, type 2 diabetes mellitus; CACS, coronary artery calcium score; CAD, coronary artery disease; N, number

Table 2. Laboratory findings in both groups

Variable	DM2 (YES/NO)	N	M	IQR	Min.	Max.
PTL (Z=-0.604; p=0.546)	NO	35	230.00	216.00-273.00	144.00	322.00
	YES	36	248.00	215.00-289.50	65.00	411.00
	Total	71	240.00	216.00-289.00	65.00	411.00
MPV (Z=-1.647; p=0.100)	NO	35	8.50	7.70-9.00	7.00	11.30
	YES	36	8.75	8.10-9.45	6.10	11.00
	Total	71	8.50	7.90-9.20	6.10	11.30
Cholesterol (Z=-2.833; p=0.005)	NO	31	4.10	3.70-4.70	2.90	6.29
	YES	41	5.10	4.41-6.20	2.20	8.60
	Total	72	4.60	3.80-5.94	2.20	8.60
HDL (Z=-1.546; p=0.118)	NO	30	1.12	0.92-1.48	0.80	2.10
	YES	34	1.30	1.17-1.58	0.70	3.94
	Total	64	1.26	1.01-1.50	0.70	3.94
LDL (Z=-2.234; p=0.025)	NO	30	2.31	2.10-2.70	0.86	4.30
	YES	34	3.00	1.92-3.73	0.70	5.50
	Total	64	2.48	1.98-3.10	0.70	5.50
Triglycerides (Z=-1.011; p=0.312)	NO	31	1.74	1.44-2.21	0.60	3.10
	YES	39	2.01	1.35-2.50	0.60	4.66
	Total	70	1.80	1.38-2.23	0.60	4.66
Ca (Z=-0.698; p=0.485)	NO	30	2.34	2.27-2.47	2.11	2.72
	YES	29	2.33	2.25-2.43	2.02	2.60
	Total	59	2.33	2.25-2.43	2.02	2.72
Uric acid (Z=-2173; p=0.030)	NO	32	275.50	245.00-332.50	217.00	464.00
	YES	28	330.00	276.00-356.50	194.00	510.00
	Total	60	292.50	252.00-347.00	194.00	510.00
CRP (Z=-0.058; p=0.954)	NO	34	3.00	2.00-5.00	0.60	9.10
	YES	37	2.90	2.00-4.50	0.50	14.70
	Total	71	3.00	2.00-5.00	0.50	14.70

N, number; M, median; IQR, interquartile range; Min., minimum; Max, maximum; Z, Z score; PTL, platelet count; MPV, mean platelet volume; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Ca, calcium; CRP, C-reactive protein; DM2, type 2 diabetes mellitus

group were slightly older than those in the non-diabetic group, this difference was not statistically significant (p=0.052).

Calcium score values in the non-diabetic group had a median of 15, with an IQR=1-85 (minimum of 0, and a maximum of 3004). The calcium score values in the diabetic group had a median of 204, IQR=20-586, with a minimum of 0 and a maximum of 3748. It was found that patients in the T2DM group had statistically significantly higher calcium score values compared to the non-diabetic group (p=0.0001)

Patients in groups I, II, and III (with a calcium score of up to 99, which represents patients without cardiovascular risk, with minimal or low risk) were statistically significantly more represented in the non-diabetic group than in the diabetic group (p=0.0001). Patients in groups IV, V, and VI (with calcium score values over 100, which represents patients with moderate, high, or very high cardiovascular risk) were statistically significantly more represented in the T2DM group than in the non-diabetic group (p=0.0001) (Table 1).

Regarding laboratory parameters, our analysis showed that significantly higher values of total cholesterol, LDL, and uric acid were measured in the T2DM group (p=0.005, p=0.025, and p=0.03 respectively). For other laboratory parameters monitored, no statistically significant difference was found between the groups (Table 2).

A correlation analysis of the influence of the variables: age, gender, PTL, MPV, total cholesterol, HDL, LDL, triglycerides, Ca, uric acid, and CRP on the calcium score values was performed. The analysis revealed that only the age showed a statistically significant correlation with the calcium score values (r=0.442; p=0.001). This was reflected in a moderate correlation with age, with older patients being 44.2% more likely to have a higher calcium score (Figure 1).

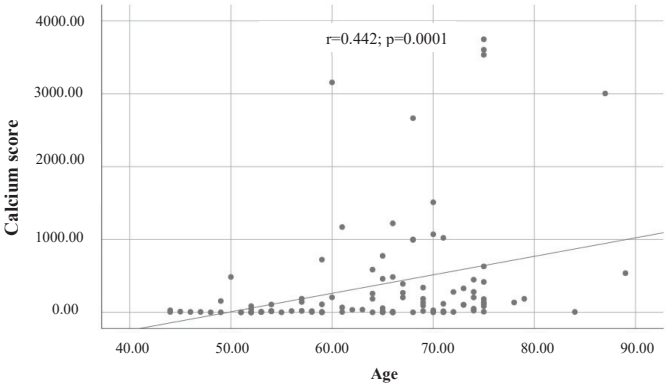

Figure 1. Correlation analysis of the influence of age on calcium score values

DISCUSSION

The main findings of our research affirm that calcium score values were significantly higher in patients with diabetes compared to those without diabetes. Also, the representation of patients with calcium score values above 100 was significantly higher in the group of diabetes patients. Furthermore, a statistically significant moderate positive correlation was found between age and the value of the calcium score, which indicates a trend of progressive increase in the value of the calcium score with increasing age of the patients.

In the present research, females were more represented in both groups (82.1% in the group of patients without T2DM and 56.9

% in the T2DM group); however, a statistically significant difference in gender distribution was found only in the group of patients without T2DM. In a cross-sectional observational study of a similar design, it was found that females predominated in the group without T2DM (67.5%), while males were more prevalent in the T2DM group (57.5%), which partially aligns with the findings of our study (17). The Framingham study showed that males with diabetes had twice the risk of cardiovascular mortality, while females with diabetes had a staggering four times the risk, compared to those without diabetes (18).

In this study, patients with diabetes were slightly older than patients without diabetes. The mean age of patients in the T2DM group was 66.04±9.68 years, while in the non-diabetic group it was 62.41±10.04 years, but this difference was not statistically significant. In a study involving 1123 patients, similar results were observed, with the average age of participants being 61.4±9.1 years, which aligns with the findings of this study (19). Similar findings were observed; the largest number of patients was in the age group of 50 to 60 years (17).

Calcium score values in this study were significantly higher in patients with T2DM. The median value in the non-diabetic group was 15, whereas in the T2DM group it was 204. Similar findings were reported, with median values of 9 and 50, respectively (20). This might be attributed to chronic high blood sugar levels, causing persistent inflammation and damage to blood vessel walls, promoting calcium build-up in the arteries (21). In T2DM, insulin resistance further alters blood vessels, encouraging calcification and leading to a high calcium score that we observed (22). Reportedly, the proportion of patients without T2DM was higher in the groups with minimal and low risk for cardiovascular events, i.e., in patients with calcium scores below 100; however, with an increase in calcium scores >1000, the proportion of patients with T2DM also increases significantly (20). Our results confirm this trend, only 1.8% of patients without T2DM had a calcium score >1000, while in the T2DM group, it was 21.6%, making this group highly at risk for unwanted cardiovascular events. Similar results were observed, with nearly half of the patients (43%) having calcium scores >400 (23). In our study, the prevalence of patients with diabetes with calcium score >400 was 35.3%, further confirming the association between diabetes and elevated calcium scores.

Our results showed significantly higher values of total cholesterol, LDL, and uric acid in patients with T2DM compared to patients without T2DM. Diabetic patients, especially when it is poorly regulated, exhibit insulin resistance that leads to numerous metabolic disturbances, primarily disrupting lipid metabolism, resulting in elevated total cholesterol and LDL levels, key contributors to atherosclerosis and increased cardiovascular risk (24). Uric acid is a notorious proinflammatory substance leading to impaired renal function, further increasing cardiovascular risk in T2DM patients (25). Among 576 individuals, including 192 with a history of T2DM and atherosclerosis, the results showed that patients with T2DM had elevated triglycerides, total cholesterol, and LDL, as well as decreased HDL values, compared to those without T2DM, which aligns with the findings of this study. The authors concluded that dyslipidaemia is a strong predictor of cardiovascular morbidity and mortality in patients with T2DM (26).

Numerous studies have examined the association between serum uric acid and T2DM, but the results have been conflicting. It was reported that patients with prediabetes and diabetes had lower mean serum uric acid values compared to patients without T2DM (27). On the other hand, a positive correlation between elevated serum uric acid levels and diabetes was found (28-30). In contrast, no significant association between serum uric acid levels and diabetes was reported (31). These results indicate the need for further studies on larger patient samples to more precisely determine the relationship between diabetes and uric acid levels.

In our study, a positive correlation was found between the calcium score and the age of the patients. These findings indicate that with increasing age, there is a progressive increase in the calcium score, which can be explained by the progression of the atherosclerotic process, loss of elasticity, and increased stiffness of the arteries (32). Similarly, it was shown that the extent of coronary artery calcification is strongly associated with age in males and females up to the ninth decade of life, and that it represents a significant cardiovascular risk factor (33). Additionally, our findings are in line with the results of a study in which, besides an addition to confirming the positive correlation between the calcium score and the age of the patients, both calcium deposits in the coronary arteries and patient age can serve as an additional prognostic marker for a more precise distinction between lower and higher risk of coronary heart disease in the elderly (34).

Limitations of this study include a relatively small sample, which may affect the generalisability of the results to the wider population. Also, patients with T2DM were included in the study, regardless of the therapeutic protocol, which may represent variability in the results due to possible differences in metabolic control and therapeutic approach.

In conclusion, this is the first research of this kind conducted in Bosnia and Herzegovina, which gives it special importance in the context of understanding the connection between coronary artery calcification and T2DM in the local population. To further confirm these findings and enable their broader interpretation, further research on larger and more heterogeneous samples is necessary.

AUTHORS CONTRIBUTION

Statement: Conceptualization, M.B., and Z.B.J.; Methodology, M.B., Z.B.J., and E.B.; Software, M.B., and M.B.; Validation, E.B., M.B., and S.P.; Formal analysis, M.B., and Z.B.J.; Investigation, M.B., Z.B.J., E.B., S.P., F.Z., A.A..; Resources, Z.B.J and A.B.; Data curation M.B. and Z.B.J.; Writing—original draft preparation, M.B., and Z.B.J.; Writing— review and editing, E.B., M.B., S.P., F.Z., and A.B.; Visualization, M.B., A.A.; Supervision, S.P., and F.Z.; Project administration, funding acquisition, M.B., and Z.B.J. All authors have read and agreed to the published version of the manuscript.

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TRANSPARENCY DECLARATION

Conflicts of interest: None to declare.

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