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Low-density lipoprotein-cholesterol and its relation to epicardial fat volume in patient with type 2 diabetes mellitus

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ABSTRACT

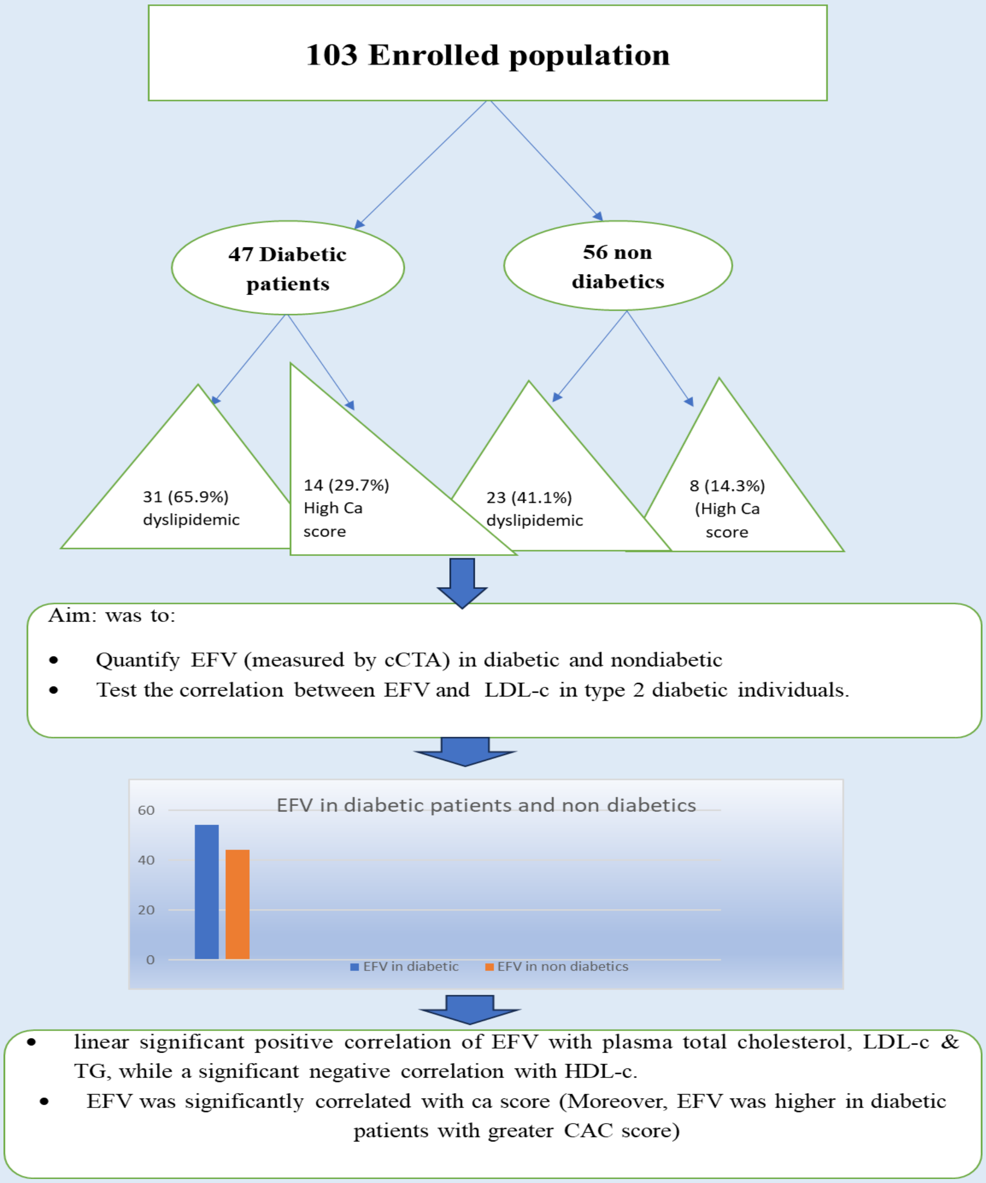
Objectives: This study aimed to compare EFV between diabetic and non-diabetic subjects in patients with clinical indications of CCTA and test the correlation between low-density lipoprotein-cholesterol (LDL-C) and EFV in type 2 diabetic (T2DM) patients.

Methods: This study was conducted on 103 cases with chest pain and intermediate risk probability for CAD and was scheduled for CT coronary angiography divided into 47 diabetic patients and 56 non-diabetic patients. The total serum cholesterol, LDL-C, TG, and HDL-C levels were analyzed for each patient. MDCT to assess CACS and EFV for patients included in the study.

Results: The results showed that plasma total cholesterol, TG, and LDL-C were higher with decreased HDL in the diabetic patient. EFV was significantly higher in diabetic patients (54.5±14.9 vs 44.7±7.7, p <0.02). EFV had a significant Linear correlation with plasma total cholesterol, LDL-C, and TG. In contrast, there is a significant negative correlation between EFV and HDL-c. EFV was significantly correlated with ca score (EFV was higher in diabetic patients with greater CAC score).

Conclusion: EFV is rising in type II diabetic patients, especially those with high ca scores, and correlates well to their characteristic hyperlipidemia, especially LDL-C. So, all diabetic patients must be started on primary prevention against LDL-C to reduce the risk of atherosclerosis.

Keywords: Type II DM, Epicardial fat volume, LDL-c.



INTRODUCTION

Diabetes mellitus (DM) is a widespread health issue that is on the rise everywhere in the globe [1] and is regarded as a classic cardiovascular risk. Cardiovascular disease (CVD), particularly coronary artery disease (CAD), is the most frequent consequence of type 2 diabetes mellitus (T2DM), with an increased mortality rate caused by systemic atherosclerosis [2]. Dyslipidemia is also frequently seen in diabetes mellitus (DM) because the routes for lipid metabolism are affected by both insulin resistance and insufficiency [3]. Increased levels of triglycerides (TG), reduced levels of high-density lipoprotein cholesterol (HDL-C) and raised levels of low-density lipoprotein cholesterol (LDL-C) are typical abnormalities of lipids seen in T2DM [4, 5]. About 15% of the weight of the heart is made up of epicardial adipose tissue (EAT), a fat-storage tissue placed underneath the pericardium [6]. As a possible therapeutic target for primary prevention, epicardial adipose tissue may be a significant imaging biomarker for obstructive CAD [7]. Patients with diabetes were shown to carry more EAT [8]. Additionally, statin medication and significant lifestyle changes have been shown to EAT accumulation and impact the inflammatory profile [9], making EAT a valuable measure for the primary prevention of obstructive CAD concurrently lower.

Aim of the study: This study aimed to compare EFV (measured by cardiac CT angiography) in diabetic and non-diabetic individuals with a clinical indication for CCTA. Additionally, we aim to study the relationship between EFV and hyperlipidemia, particularly LDL-C in T2DM.

SUBJECTS AND METHODS

Methods: This retrospective cross-sectional observational study involved patients with T2DM who were scheduled for CT coronary angiography between March 2021 and April 2022 due to ambiguous stress test results or the presence of multiple cardiovascular risk factors and suspected coronary artery disease. The patients with known allergies, renal insufficiency, serum creatinine more than 1.4 mg/dl, pregnancy, or patients with irregular heartbeats (as arrhythmia, AF, frequent PVCs) were excluded. Other exclusion criteria for this study included those with congenital heart disease, history of open-heart surgery, valvular heart disease, post-valvular replacement, pericardial effusion, high coronary calcium score (> 1000), and those with pacemakers or other cardiac devices.

The Cardiology Out-patient Clinic provided the cases for the study. In accordance with the rules established by the Al-Azhar University Ethical Committee, Cairo, Egypt, all participants were told of the study's goal before giving verbal consent.

Cardiovascular risk factors were assessed using demographic and biometric data such as gender, age, and smoking behavior. A self-reported history of diabetes, fasting plasma glucose of more than ≥126 mg/dl, and/or the use of blood glucose-lowering medicines (oral hypoglycemics or insulin) were all considered as a diagnosis of diabetes mellitus [10]. All individuals had their height and weight assessed, and BMI was determined as weight (kg)/height (m^2). The lipid profile was the focus of the laboratory examination. An automated analyzer performed an enzymatic test to determine total serum cholesterol levels, TG, LDL-C, and HDL-C.

Multi-detector computed tomography study: Retrospective data from the picture archiving and communication system (PACS) was obtained for the patients who underwent CCTA. Every CT scan was done on the second generation dual-source 64-slice CT scanner Somatom Definition Flash (SEMINS Medical Solution VA44A, Forchheim, Germany), which has the following features: acquisition (2 x 128), rotation speed of 0.28 seconds, generator power of 200 KW, table load of 300 kg/660 lb, and scan range of 200 cm. Tomograms were taken during a single breath-hold in a cranio-caudal orientation from the tracheal bifurcation to the diaphragm. The following conditions were used for CT scanning: spiral mode for retrospective ECG-gated acquisition. Axial pictures were retroactively reconstructed at an ideal window using a three-dimensional workstation.

A multiplanar reformatted picture was used to analyze the image data sets (vertical, short axis, and long axis), curved multiplanar reformatted pictures, thin-slab maximum-intensity projections, and volume-rendered pictures. Two-dimensional reconstructions (curved multiplanar reformation) of the coronary arteries were performed to determine their patency. This 2-dimensional image shows the vessel's wall, lumen, and surrounding tissue. The continuity of contrast material throughout the vessel shows its patency when at least two orthogonal reconstruction planes are used.

Measurement of Epicardial Fat Volume (EFV): A standard scanning methodology was used to evaluate epicardial fat volume. The EFV was calculated in non-contrast cardiac CT by summating the epicardial adipose tissue areas considered from the pulmonary trunk to the diaphragm. Adipose tissue located between the myocardium's surface and the pericardium's visceral layer is known as epicardial fat. Every fourth slice was manually traced from the aortic root to the apex using axial slices that were 5.0 mm thick. After manually tracing each slice between the manual slices, the computer program automatically interpolated and calculated the EFV in cm^3. There were 30 to 40 slices per heart. The accuracy of automatically traced slices was checked. A -30 to -250 HU threshold attenuation value was used to identify fat voxels.

Quantification of coronary calcifications: An initial non-contrast CT scan was performed to diagnose and quantify coronary calcifications from the carina to the apex. Each patient's total coronary calcium score was calculated.

Statistical analysis: To accomplish the statistical analysis, SPSS Inc., Chicago, IL, USA, version 16.0 was used. A mean ± standard deviation was calculated for each of the data points. In categorical data, absolute frequencies and percentages are presented. To examine differences between groups, unpaired t-tests were used to compare numerical data. In order to assess any potential relationships, Pearson correlation coefficients were used [11].

RESULTS

The enrolled population was 103 cases with a mean age of 56.9 ± 9.5 years divided into 47 diabetic patients (group I) with an average age of 55.1 ± 5.8 years old and 56 non-diabetic patients (group II) with an average age of 58.5 ± 4.0 years old. Male patients dominated the diabetic patient group at around 95%. The non-diabetic patients were slightly older but to an insignificant extent (58.5± 4.0 vs 55.1± 5.8, p-value 0.06). Diabetic patients had a higher prevalence of dyslipidemia than non-diabetics. Table 1 shows that diabetic patients had higher BMIs than non-diabetic patients.

Table 1. Comparison between Baseline demographic and clinical characteristics of the study population

Variables	Group I (n= 47)	Group II (n=56)	P value
Age (years)	55.1 ± 5.8	58.5 ± 4.0	0.06
Male sex (%)	43/47 (91.5%)	50/56 (89.2%)	0.707
Height	171.90 ±6.7	171.00 ±7.6	0.5
Weight	88.2 ± 9.3	90.50 ± 12.1	0.2
BMI	31.0 ±7.9	31.0 ±4.7	0.9
Dyslipidemia (%)	31/47 (65.9%)	23/56 (41.1 %)	0.012
Active Smoking (%)	16/47 (34.04%)	19/56 (33.9%)	0.990
HTN %	----	31/56(55.3%)	----------
DM duration in years	6.5±4.3	----	---------

Total plasma cholesterol, LDL-cholesterol, and TG were insignificantly higher in the diabetic patient group versus non-diabetic. Table 2 shows diabetic patients have decreased HDL compared to non-diabetic patients.

Table 2. Comparison between both groups as regards lipid profile

Variable	G I (n=47)		G II (n=56)		P value
	Mean	SD	Mean	SD	
Lipid profile					
Plasma total cholesterol (dl/l)	215.4	64.6	205.5	59.2	0.4
LDL cholesterol	136.7	51.0	128.4	50.3	0.4
HDL cholesterol	41.5	7.6	43.6	7.5	0.1
Triglyceride	189.9	97.4	167.4	77.7	0.2
LDL/HDL ratio	3.29	6.7	2.9	6.7	0.6
TC/HDL ratio	5.19	8.5	4.7	7.8	0.7

Multi-detector computed tomography (MDCT) data: Diabetic patients had significantly higher EFVs (54.5±14.9 VS. 44.7±7.7). In Table 3, diabetic patients were more likely to have CCS > 400 (29.7% vs. 14.3%, p = 0.01) than non-diabetics.

Table 3. Comparison by CT angiography for measurement of EFV and high Ca score of the studied group.

Variables	G I (n=47)		G II (n=56)		P value
	Mean	SD	Mean	SD	
EFV (ml)	54.5	14.9	44.7	7.7	0.02
High CAC score >400	14/47 (29.7%)		8/56 (14.3%)		<0.01

Abbreviations: EFV epicardial fat volume

Correlation of EFV with lipid profile, especially LDL-c and CAC score: Linear correlation between the EFV determined by CT angiography with age and BMI was significant (r=0.24, p<0.00001), (r=0.10, p<0.0001), respectively. The EFV was inversely correlated with smoking (r=-0.06, p<0.001).

Moreover, the linear correlation of EFV with plasma total cholesterol, LDL-cholesterol, and TG was significant; however, EFV and HDL-cholesterol had a significant negative correlation. EFV was significantly correlated with ca score (Moreover, EFV was higher in diabetic patients with greater CAC score) as shown in Table 4.

Table 4: Correlation between EFV and Ca score, risk factors including lipid profile.

Variables	EFV (r)	P value
Age	0.24	<0.00001
BMI	0.10	<0.0001
Smoking	-0.06	0.001
Dyslipidemia	0.29	0.17
LDL cholesterol	0.15	<0.0001
HDL cholesterol	-0.20	<0.0001
Triglycerides	0.20	<0.001
Total cholesterol	0.15	<0.0001
CAC SCORE	0.34	<0.001

DISCUSSION

Both in wealthy and emerging nations, Type II DM is rising quickly [12]. It is well recognized that type II DM raises the risk of cardiovascular disease [13], notably in individuals with acute coronary syndrome [14] and increases mortality. Given that diabetic individuals may have myocardial ischemia in an unusual or asymptomatic pattern, early risk assessment and prediction are crucial. This results in optimizing cardiovascular disease therapy, which reduces morbidity and mortality [15].

According to this research, type 2 diabetes individuals had greater lipid profiles than non-diabetic patients, however, this difference was not statistically significant. These results are consistent with earlier research that indicates that lipoprotein abnormalities are more prevalent in diabetes participants than in non-diabetic ones [16, 17]. Additionally, diabetic individuals in this research had lower HDL-c levels than non-diabetic patients. As shown in prior research, HDL decreases the body's cholesterol pool by improving cholesterol clearance from peripheral tissues. Low plasma HDL-C levels were often linked to type 2 diabetes [18, 19].

As shown in this research as well as in other studies, declining HDL-C concentrations are often accompanied by high TG levels, and this combination has been firmly linked to an enhanced risk of coronary artery disease (CAD) [20, 21]. The thicker LDL particles mostly absorb these HDL esters, thus lowering HDL-C levels. Additionally, the hepatic lipase enzyme efficiently metabolizes HDL-C into smaller particles that are quickly removed from the plasma [22, 23].

In T2DM, there is a relative insulin shortage, resulting in lower HDL-C levels and higher TG levels. Better glycemic control may alleviate these conditions [24]. In T2DM patients, insulin resistance-linked lipoprotein lipase deficiency and a decrease in HDL2 subfraction are the most common causes of HDL hypocholesterolemia [25].

TC and LDL-C levels in T2DM may not differ statistically from those in non-diabetics, according to the UK Prospective Diabetes Study [26, 27].

The TC/HDL ratio in this study was 5.2 ± 8.5 in diabetic individuals, which is consistent with another research that found the TC/HDL-C ratio to be a sensitive and specific indicator of cardiovascular [28]. In addition to HDL-C, the TC/HDL-C ratio is recognized as a predictor of the risk of CHD, particularly with levels >6.0 [29].

A higher fasting TG concentration was found in T2DM compared to non-diabetics in this study, although this difference was not statistically significant. To form very low-density LDL-C particles devoid of cholesteryl esters, high TG levels enhance the transfer of cholesteryl esters from LDL-C and HDL-C to very VLDL-C through the cholesteryl ester transfer protein [30]. Atherogenesis is brought on by the artery wall macrophages consuming these tiny, dense lipoprotein particles [31].

Different diabetic people are at risk for CVD. To provide the best care for them, it is crucial to separate the low risk from the high-risk groups [32, 33]. In addition to conventional cardiovascular risk variables, EFV assessment has additional relevance in predicting atherosclerotic CAD in T2DM.

In this research, people with diabetes showed higher CCS values (>400) than those without diabetes. This is consistent with the findings used MDCT coronary angiography to examine the usefulness of CCS as a marker of severe CAD in the asymptomatic Spanish population [34]. Diabetic individuals had a higher CCS. CAC assessment is an effective tool for assessing the severity of coronary artery disease. Significant CAD was predicted by CCS >300 [35].

According to research by Farrag, *et al.* [36], T2DM patients have a greater coronary calcific load for CAD prediction. The CCS of T2DM patients was found to be greater than that of non-diabetics, making them a better candidate for CAD risk assessment [37, 38].

Additionally, the present research found that diabetes individuals had greater EFV than non-diabetic patients. This was consistent with research by Yun et al., which discovered a link between pericardial fat content and diabetes [39].

This research's findings agree with those of Wang et al., who examined 78 non-diabetic controls and 49 patients with T2DM and utilized MDCT to evaluate coronary lesions, EFV, and CCS. They discovered that T2DM patients had considerably higher EFV than non-diabetic controls (166.1 ±60.6 cm^3 vs. 123.4 ±41.8 cm^3, P <0.0001) [40].

Furthermore, this research supports Konishi, *et al.* [41] findings that the volume of pericardial fat and DM markers were positively correlated in patients with suspected CAD. Additionally, this research supported by Mahabadi, *Et al.* [42] revealed that 4093 people with a frequency of 12.4% of diabetics had EFV and DM association.

Age (r=0.24, p<0.00001), BMI (r=0.10, p<0.0001), and smoking (r=-0.06, p<0.001) all significantly correlated with the EFV, which is also consistent with earlier research that found the EFV was directly correlated with the presence of cardiovascular risk factors in populations without a history of CAD [43]. In line with earlier research, classic cardiovascular risk factors, including smoking, hypertension, diabetes, and male gender, are all significantly associated with epicardial fat [44].

However, there was a negative correlation between EFV and HDL cholesterol, which was consistent with earlier research that showed an association between EFV and triglycerides [45]. As in previous research, EFV exhibited a significant positive correlation with plasma total cholesterol, LDL cholesterol, and triglyceride.

Therefore, EAT may be changed to reduce cardiovascular risk, providing a novel strategy for primary CAD prevention [46]. The quantitative calculation of EFV may provide extra information on cardiovascular risk since, unlike BMI, it measures visceral adiposity rather than overall obesity. This straightforward EFV assessment may aid in selecting certain patients for revascularization, intensive lifestyle adjustment, and high-dose statin medication when necessary.

CONCLUSION

EFV has risen in T2DM patients, especially those with high CA scores in multi-detector CT, and correlates well to their characteristic hyperlipidemia, especially LDL-c. So, to reduce the risk of atherosclerosis in diabetic patients, primary prevention must be initiated.

Limitations and Futures

The number of cases was relatively low, so many studies are recommended. Relation of Duration of diabetes should be included with different values of EFV for each to avoid heterogeneity of groups. The level of HBA1c and its correlation to EFV values should also be included.

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Abbreviations: DM: Diabetes mellitus, CVD: Cardiovascular disease CAD: coronary artery disease, T2DM: type 2 diabetes mellitus, TG: triglycerides, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, EAT: epicardial adipose tissue, BMI: Body Mass Index, MDCT: Multi-detector computed tomography., EFV: epicardial fat volume, r: Pearson correlation

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