

## Correlation between Dyslipidemia and The Severity of Coronary Artery Disease Using SYNTAX Scoring System

Mostafa M. Abdelrazik, Ezz El Din El Sawy, Ahmed M. Fahmy, Fouad Rafik.

Department of Cardiology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

### ABSTRACT

**Background:** the relationship between hyperlipidemia and an increased risk of coronary heart disease has been well documented and has served as a motivating factor for research into lipoproteins structure, function and metabolism. Many epidemiological studies have revealed that chronically elevated lipid and cholesterol levels are associated with an increased incidence of atherosclerosis. Dyslipidemia together with hypertension and diabetes is major modifiable risk factors for atherosclerotic disease and the subsequent development of cardiovascular events. Dyslipidemia is known to be an independent predictor for cardiovascular events, other risk factors including family history, hypertension, tobacco use, age, sex and diabetes also have been found to be associated with an increased risk of coronary artery disease (CAD). This cross-sectional study was aimed to investigate the association of Dyslipidemia as an atherosclerosis predictor and its relationship to the severity of CAD using SYNTAX score. **Patients and Methods:** the current study included 535 patients who presented during 2015 with chest pain to Dar Al Fouad Hospital, experiencing symptoms of CAD or evidence of CAD by noninvasive testing were enrolled, a fasting blood sample was extracted and assessed for lipids profile. Patients underwent coronary angiography either using femoral or radial approach, and the resulting angiographic study was used to calculate the SYNTAX score of each patient. Patients were divided in to two group i.e. CAD and Non-CAD group. The CAD group was further divided into three sub-groups according to the SYNTAX score into low risk, intermediate risk and high risk group. **Results:** in this study, triglycerides, total cholesterol and LDL-C levels were positively associated with sever CAD and higher number of diseased vessels. Higher HCL-C levels were also found in subjects with normal coronaries. **Conclusion:** there was no significant proportionate, linear relation between the SYNTAX score and the levels of triglycerides, total cholesterol or LDL-C

**Key words:** Atherosclerosis, SYNTAX Score, Dyslipidemia, CAD, Non-CAD.

### INTRODUCTION

Atherosclerosis is a disease of large and medium sized arteries such as the carotid and coronary arteries, and arteries of the lower extremities. It is characterised by focal lesions of one of the following types: fatty streak, fibrous plaque, or complicated lesions. A great number of hypotheses have been published about the pathogenesis of atherosclerosis, such as the lipid hypothesis, thrombogenic hypothesis, and the endothelial cell injury hypothesis. Many epidemiological studies have revealed that chronically elevated lipid and cholesterol levels are associated with an increased incidence of atherosclerosis<sup>(1)</sup>.

The presence of Lp(a) ( a sub molecule of LDL) has emerged as a powerful genetic risk factor for coronary artery disease (CAD) raising the question of Dyslipidemia and its relation to CAD<sup>(2)</sup>. Lipoprotein (a) (Lpa) is a complex molecule of low-density lipoprotein (LDL) to which a large, hydrophilic glycoprotein, apolipoprotein (a) [Apo(a)], is covalently linked via disulfide bonds. Based on its structure, Lp(a) has both atherogenic and prothrombotic properties<sup>(3)</sup>

Triglycerides (TG) rich lipoproteins, which originate both in the intestines and liver, are considered as atherogenic factor<sup>(4)</sup>. The aim of this study was to evaluate, in judging the severity of CAD, the association between the levels of lipid profile parameters as a biomarker.

Patients and methods:

A cross-sectional study was conducted on 535 patients who underwent coronary angiography between January 2015 and December 2015 at Dar Al Fouad Hospital. The study was approved by Al Azhar University and Dar Al Fouad Hospital. Informed consent was taken from patients. The patients' demographic profiles, socioeconomic status, personal habits, and disease risk factors histories were recorded. Blood pressure (BP) was measured before the patients were sent to the catheterisation laboratory. Patients with a history of chest pain, angina, ST-elevation acute coronary syndrome, non ST- elevation acute coronary syndrome and stable angina were included. All patients received long-term treatment with angiotensin-converting-enzyme (ACE) inhibitors, calcium (Ca) antagonists, or  $\alpha$ - and  $\beta$ -adrenergic blocking

agents. Patients with nephrotic syndrome, acute or chronic renal failure, thyroid disorders, acute infections, stroke, or diabetic ketoacidosis were excluded.

Coronary angiography was performed using a radial approach. Coronary angiography results were evaluated by interventional cardiologists. The complexity of CAD was determined by an angiographic grading tool—the synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) score <sup>(5)</sup>. In principle, the SYNTAX score is the sum of the points assigned to each individual lesion identified in the coronary tree with >50% narrowing in the diameter of the vessels that measure greater than 1.5 mm. The percentage of stenosis was not a consideration. Only the presence of a stenosis from 50–99% in diameter, a narrowing of less than 50% in diameter, or a total occlusion were considered. The entire patient group was divided into two subgroups: subjects with CAD who had a SYNTAX score >0 and subjects without significant coronary artery stenosis with a SYNTAX score of 0.

Fasting blood samples were collected after a 10 to 12 hour fast and before cardiac catheterisation for all patients except the ST-elevation acute coronary syndrome lipid samples were collected after. Samples were taken in sterile tubes, centrifuged at 3000 rpm for 10 minutes at 4°C, and then the separated serum stored at -80°C until assayed. Serum total cholesterol, high-density lipoprotein cholesterol (HDL-C), LDL-cholesterol (LDL-C) and TG levels were estimated by standard methods. The results are presented in mean and standard deviation (SD) and percentage. The *P* value <0.05 was considered significant. All the analysis was carried out by using the Statistical Package for the Social Sciences (SPSS). T- test was used to compare the results.

## RESULTS

Angiography revealed that 429 patients had proven CAD, the triglycerides level was significantly (*P*=value 0.004) higher in the CAD ( $173 \pm 110.8$ ) mg/dl compared to the non-CAD group (Table 1). The HDL-C was significantly lower in the CAD group ( $36 \pm 10.1$ ) mg/dl than the non- CAD group. The total cholesterol level was significantly (*P*-value 0.026) higher in the high risk group of CAD ( $203 \pm 61.9$ ) mg/dl compared to the other groups. Also the LDL-C was significantly (*P*-value 0.005) higher in the high risk group of CAD ( $136.2 \pm 56.6$ ) mg/dl compared to the other groups. It was also noted

that a higher level of triglycerides ( $197 \pm 57$ ) mg/dl was found in patients with three vessel disease compared to other patients (*P*-value <0.001) (Table 3). Finally a higher HDL-C ( $40 \pm 9$ ) mg/dl was found in patients with normal coronaries with a significant *p*-value <0.001. On further analysis of the CAD group (Table 2), they were subdivided in to three sub groups according to syntax score. It was noted that most of the patients fell in the low risk group of syntax score (< 23) constituting about (66.7%) of the CAD group. The low risk group also had lower mean LDL-C of ( $117.8 \pm 43.6$ ) mg/dl compared to ( $136.2 \pm 56.6$ ) mg/dl the high risk group with significant *p*-value of (0.005). Also significantly lower total cholesterol with mean value of ( $188.6 \pm 53.2$ ) mg/dl compared to the high risk group ( $203 \pm 61.9$ ) mg/dl with *p*-value of (0.026). There was no significant difference between the groups regarding the VLDL-C and the lipid risk ratios. It was noted that the commonest ECG presentation for the low risk group was inferior changes with percentage of (25.2%). On the other hand the most common ECG presentation for the high risk group was antro-lateral changes with percentage of (32.9%).

However despite the significant differences between the groups it was noted that there is weak correlations between severity of CAD and all the lipid profile parameters, with  $r=0.04$  when correlating Syntax score with LDL-C,  $r=0.01$  when correlation Syntax score with total cholesterol and  $r= -0.04$  when correlating syntax score with HDL-C.

## DISCUSSION

In the current study, higher levels of TG and VLDL were not only associated with the presence of coronary disease but also with the severity of the coronary atherosclerosis. This was concordant with previous studies <sup>(6)</sup>. Higher TG levels in our patients appeared to contribute to CAD risk, with mean TG levels of ( $173 \pm 110$ ) mg/dl were strongly associated with the extent of a patient's coronary atherosclerosis; therefore, the present coronary angiography proven study is in agreement with the documented epidemiologic observations reported in previous studies, which was that hypertriglyceridemia commonly increases CAD in patients <sup>(7)</sup>. However, our study showed low levels of TC and LDL-C in CAD group ( $126.5 \pm 51$ ) mg/dl compared to non-CAD group ( $196.4 \pm 61.3$ ) mg/dl. Which was discordant with the general consensus and previous studies <sup>(8)</sup>. It was noted that risk ratios (TC/HDL and LDL-C/HDL-C) showed no

significant difference between the two groups. Which is also discordant with the general consensus and previous studies<sup>(8)</sup>. This may be due to presence of higher number of patients in the non-CAD group with lipid profile parameters in upper normal range. Our findings can be due to the use of statins or possibly the impact of healthy diet and the physical activity on the lipid profile parameters which was proven in previous studies<sup>(9)</sup>.

It was also noted that, lower levels of HDL-C were found to be associated with the severity of CAD and increasing severity as suggested in previous studies (10). The mean HDL-C was significantly lower p-value of (0.001) in the non-CAD (39.8±14) mg/dl compared to the CAD group (36±10.1) mg/dl<sup>(10)</sup>. When dividing the patients according to the severity of CAD using syntax score, we found that TC was significantly p-value of (0.02) higher in the high risk group with mean (203±61) mg/dl compared to mean of (188.6±53.2) mg/dl in the low risk group (Table 2). Also, HDL-C was significantly p-value of (<0.001) higher in the high risk group with a mean value of (39.1±10) mg/dl compared to low risk group with mean value of (35.8±10.2) mg/dl (Table 2). It was noted that the TG level was highest in the low risk group with mean of (181±123) mg/dl as compared to the high risk group with mean value of (151.5±75.9) mg/dl. These findings are not consistent with previous research or studies<sup>(7)</sup>.

Although the LDL-C was significantly p-value of (0.005) higher in the high risk group compared to the low risk and intermediate risk groups, there was weak linear correlation between the two variables ( $r = 0.04$ ). Also there was weak correlation between the groups with respect to TG with ( $r = 0.05$ ), TC ( $r = 0.01$ ) and HDL-C ( $r = -0.04$ ). On the other hand, a previous similar study showed a significant p-value of (<0.0001) correlation between severity of CAD and elevated levels of LDL-C  $r = 0.7$  which was discordant with our findings<sup>(6)</sup>.

On comparing the grades of diseased vessels, we found that higher TG (197±57) levels and very low HDL (30±6) levels in multivessel (MVD) patients as compared to those with normal coronary (NC) status with a significant p-value of (<0.001) for both. These findings are concordant with the previous study<sup>(6)</sup>.

## CONCLUSION

In this study, triglycerides, total cholesterol and LDL-C levels were positively associated with

sever CAD and higher number of diseased vessels. Higher HCL-C levels were also found in subjects with normal coronaries. However there was no significant proportionate, linear relation between the SYNTAX score and the levels of triglycerides, total cholesterol or LDL-C.

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Tables:

**Table.1** Comparison between the two groups against several lipid profile parameters, BP readings, HBA1c , BMI and EF.

Parameters \ Groups	Non-CAD (syntax score = 0) (n=106 patients)	CAD ( Syntax score > 0) (n=429 patients)	P value
TG (mg/dl)	141± 79.2	173 ± 110.8	NS
TC (mg/dl)	196.4 ±61.3	190.3±54.5	NS
HDL-C (mg/dl)	39.8±14	36±10.1	NS
LDL-C (mg/dl)	126.5±51	120.9±46.3	NS
VLDL-C (mg/dl)	30.1±19.1	34.2±20.7	NS
TC/HDL-C ratio	5.5±2.92	5.53±1.83	NS
LDL-C/HDL-C ratio	3.66±2.48	3.51±1.51	NS
BMI (kg/m <sup>2</sup> )	26.1±2.7	31.1±2.1	NS
HBA1c %	6.5±2	7.1±2.4	NS
EF by M-mode	52.1±15	46.1±15	<0.0001
DM (%)	37.5%	58.2 %	<0.001
HTN (%)	56.3%	64.5%	NS
Smoker	34.8%	56.5%	<0.001
Ex-smoker	25.9%	26%	NS
Use of Statins	46.4%	54.8%	NS
Male Gender	68.8%	91.5%	<0.001
BMI > 18.5	97.9%	92.5%	NS
History of IHD	20.5%	35%	NS
ECG changes	45.7%	77.5%	<0.001

**Table.2** Sub-categorizing the CAD Subgroup according to syntax score against Lipid profile parameters , EF , HBA1c ,male gender, smoking, DM, HTN, dyslipidiemia and history of IHD.

Parameters \ Groups	Syntax <23 (286 patients) Low risk Group	Syntax 23-32 (64 patients) Intermediate risk Group	Syntax >32 (79 patients) High risk Group	P-value
TG (mg/dl)	181±123	159±76	151.5±75.9	NS
TC (mg/dl)	188.6±53.2	178.8±46.7	203±61.9	NS
HDL-C (mg/dl)	35.8±10.2	33.1±7.3	39.1±10.64	<0.001
LDL-C (mg/dl)	117.8±43.6	114.1±39.4	136.2 ±56.6	NS
VLDL-C (mg/dl)	35.2±22.6	31.8±15.3	31.9±15.7	NS
TC/HDL-C	5.5±1.7	5.6±1.54	5.55±2.37	NS
LDL-C/HDL-C	3.42±1.34	3.5±1.24	3.74±2.12	NS
BMI>18.5 (%)	92.5	95.7	89.8	NS
HBA1c (%)	6.8±2.2	6.7±1.8	8.9±2.5	<0.0001
EF (%)	57.5±10	52±12	49±14	<0.0001
DM (%)	53	48.4	87.3	<0.001
HTN (%)	58.7	56.3	89.9	<0.001
Smoker (%)	59.4	64.1	38	<0.001
Ex-smokers (%)	20.3	32.8	44.3	<0.001
Use of statins (%)	48.3	54.7	79.7	<0.001
Male Gender(%)	90.2	93.8	94.9	<0.001
History of IHD (%)	27.6	31.3	67.1	<0.001
ECG changes (%)	74.1	73.4	87.3	<0.001

**Table 3.** Shows comparison between the vessel disease grades and different parameters of lipid profile. (NC = normal coronary; SVD = single vessel disease; DVD = double vessel disease; MVD = multi vessel disease; TC = total cholesterol; TG = triglycerides; HDL-C = high density lipoproteins cholesterol; LDL-C = low density lipoproteins cholesterol; VLDL-C = very low density lipoproteins cholesterol.)

Parameter (mg/dl)	Vessel Grades				P-value
	NC	SVD	DVD	MVD	
TG	124±44	177±39	187±42	197±57	<0.001
TC	140±30	151±28	152±35	148±31	NS
HDL-C	40±9	31±7	31±8	30±6	<0.001
LDL-C	75±27	84±27	83±32	79±29	NS
VLDL-C	25±9	35±8	37±8	39±12	<0.001