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ASSOCIATION OF THE APOLIPOPROTEIN B/APOLIPOPROTEIN A-1 RATIO WITH THE SEVERITY OF CORONARY ARTERY DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT: Although many studies have demonstrated the importance of the apoB/apoA-1 ratio as a risk marker of atherogenicity, less is known about apoB/apoA-1 ratio in predicting and the severity of coronary artery disease (CAD) in T2DM. Our study aimed to assess possible associations between apoB/apoA-1 ratio levels and the severity of coronary artery diseases in patients with type 2 diabetes mellitus (T2DM). Plasma levels of lipidic profile components, apolipoproteins and the apoB/apoA-1 ratio were determined in 148 CAD patients with T2DM and in 159 patients with only CAD. Cut off value of the apoB/apoA-1 ratio was determined from 207 healthy subjects. Severity of CAD was quantified according to the prevalence of multivessel disease and the degree of coronary stenose. Association between the apoB/apoA-1 ratio and the severity of CAD were evaluated using the receiver operating characteristic (ROC) curve and apoB/apoA-1 ratio. ApoB/apoA-1 ratio levels didn't show significant differences between DM and NDM patients (DM: 0.9±0.5; NDM: 0.8±0.5; P=0.529). In contrast, difference was significant between these groups when patients were categorized according to low and high levels ApoB/ApoA-1 ratio. Highest levels of ApoB/ApoA-1 ratio were shown in patients with multivessel disease and significant stenose. The area under the ROC curve for ApoB/ApoA-1 in patients with T2DM was (0.513±0.041 (95% CI: 0.443, 0.594), P=0.749). The apoB/apoA-1 ratio is not associated with the severity of CAD in patients with T2DM in contrast to its high levels which might be contributed to the assessment of patients at high cardiovascular risk.

INTRODUCTION: Diabetes mellitus is a well-established risk factor for the development of coronary artery disease (CAD). Patients with type 2 diabetes mellitus (T2DM) have early onset of CAD and the involved vessels show severe disease. The CAD in diabetic patients is characterized by severe, multivessel, long segment and extensive disease [1].

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However, development of cardiovascular complications is not uniform in all patients with diabetes mellitus. Most of the diabetic populations are prone to get CAD in spite of conventional risk factors being controlled and some patients remain free of CAD despite many years of treatment for diabetes [2].

The biologic components of coronary plaques depend on the pathophysiologic mechanisms of coronary atherosclerosis and have been associated with a variety of circulating molecules linked to inflammation and metabolism [3]. In vascular disease in diabetes, the pathophysiology involves abnormalities in endothelial and vascular smooth

muscle cells, and alterations in platelet function [4]. Due to recent advances in understanding circulating molecular actions, cross-talk between adipose tissue, the immune system, and the vascular wall in T2DM, several novel biomarkers and predictive tools to aid in the appropriate intervention of CAD have been proposed [5]. Thus, it is of fundamental importance in T2DM management to determine the factors that predispose these patients to develop CAD [6]. Apolipoproteins are important components of lipoprotein particles, and there is accumulating evidence that the measurement of various forms of apolipoproteins may improve the prediction of the risk of cardiovascular disease [7]. Several steps in the metabolism of the plasma lipoproteins are regulated by insulin [6].

Apolipoprotein B (apoB) is an essential structural component of very low-density lipoproteins, intermediate-density lipoproteins, and low-density lipoproteins. Because each particle of these lipoproteins contains one molecule of apoB, the total atherogenic particles number can be accurately estimated by measuring the plasma level of this apoprotein [8]. Apolipoprotein A-1 (apoA-1) is the major apolipoprotein associated with high-density lipoprotein (HDL), and a main initiator and driver of the reverse cholesterol transport. ApoA-1 can also manifest anti-oxidant and anti-inflammatory effects, thus, apoA1 manifests several anti-atherogenic effects [9].

Emerging evidences indicate that the apoB/apoA-1 ratio is a powerful marker of risk for future cardiovascular disease [9]. Despite the clinical importance of the above lipids, lipoproteins and their ratios, the relationships between the apoB/apoA-1 ratio and the extent of CAD in T2DM have not been consistently shown.

It is fundamental to explore the features of T2DM patients with concomitant CAD that distinguishe this population from patients with CAD only. To the best of our knowledge there are little studies correlating apoB/apoA-1 ratio with the severity of CAD in T2DM. Therefore, our objectives were to investigate the possible relationship between apoB/apoA-1 ratio and the severity of CAD in patients with T2DM.

MATERIAL AND METHODS:

Population study: A total of 307 patients with CAD admitted to the Department of Cardiology University Hospital, Monastir were prospectively studied. A total of 207 healthy subjects were donors recruited from the Blood Bank Department of the University Hospital of Mahdia. T2DM was diagnosed according to the American Diabetes Association criteria. CAD was diagnosed as the presence of a luminal diameter stenosis >50% in at least one major coronary artery (left main coronary artery (LMCA), left anterior descending (LAD), left circumflex (LCx) or right coronary artery (RCA) or their major branches) by angiography. Multi-vessel CAD was defined as a disease stage in which at least two of the major coronary arteries were involved with atherosclerosis of significant severity. Angiographic measurements were not performed in healthy controls.

Study subjects were divided into two groups: patients with CAD only (n=159) and patients with T2DM and CAD (n=148). Exclusion criteria were renal failure, malignant diseases, autoimmune disorders, and inflammatory diseases. This study was approved by the Ethics Committee of Medical University, and informed consent was obtained from all participants.

Plasma collection and storage: Total cholesterol (TC) and triglyceride (TG) and HDL- cholesterol were measured by enzymatic colorimetric methods, LDL-cholsesterol was estimated by the Friedewald equation. ApoB, apoA-1, and Lipoprotein(a) (Lp(a)) measurements were carried out by means of the turbidimetric method(Cobas Integra 600, Roche). The assays were performed in the biochemistry laboratory of the University Hospital, Farhat Hached Sousse.

Coronary angiography and assessment of CAD severity: Coronary angiography was performed using standard techniques and all coronary angiograms were reported and reviewed by experienced cardiologists who were blinded to procedural and clinical data. In cases of disagreement, the final decision was reached by consensus. CAD was defined as >50% luminal narrowing of at least one major epicardial vessel. We attempted to quantify the ‘‘severity of CAD’’ by ascertaining the prevalence of

multivessel disease, extent of CAD [one, multi vessel disease stenosis(>50%)]. According to the number of diseased arteries, patients were categorized as having no disease, or one, multi vessel disease. Degree of coronary stenosis was classified according to previously published guidelines [10]: moderate: 50–70% stenosis and severe: >70% stenosis.

Statistical analysis: All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences). Continuous data are reported as mean ± standard deviation and categorical data as percentages. All statistical tests were two-sided and P values of less than 0.05 were considered statistically significant. Cut-off value for ApoB/apoA-1 ratio were determined from the healthy subjects (n=207). The cut-off value of the apoB/apoA-1 ratio was 0.9. A receiver-operating characteristic (ROC) curve analysis was drawn to identify the optimal cut-off points of ApoB/apoA-1 ratio levels (to determine maximal sensitivity and specificity) for predicting CAD in T2DM. The area under the curve (AUC) value was calculated to determine accuracy of the test.

RESULTS:

Clinical Characteristics: Among 307 subjects with CAD, 148 had T2DM. The group of DM patients comprised 94 (63.5%) men at a mean age of 60.9 ± 9.4years. Clinical characteristics and parameters of the two groups and significant differences are shown in **Table 1**.

TABLE 1: BASELINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE STUDY POPULATION

Characteristics	All Patients N=307	NDM N=159	DM N=148	p
Age(years)	60.3±11.0	59.7±12.4	60.9±9.4	0.377
Male, n (%)	230(74.3)	136(85.5)	94(63.5)	<0.001
BMI(Kg/m²)	27.5±4.3	27.3±4.2	27.7±4.4	0.462
Smoker (%)	88.2	61.9	38.1	0.002
Obesity (%)	22.6	20.4	24.7	0.595
Hypertension (%)	47.1	37.7	57.4	0.001
Dyslipidemia (%)	23.5	16.5	31.1	0.003
Personal history of CAD (%)	33.2	28.9	37.8	0.169
Vessel involved (%)				
LMCA	7.0	10.3	3.7	0.058
LCx	50.7	45.8	55.6	0.152
LAD	72.6	67.3	77.8	0.085
RCA	48.4	44.9	51.9	0.305
Stenose				
<50%	5.8	4.5	6.8	0.890
[50-70] %	27.2	27.3	27.1	
>70%	67.0	68.2	66.1	
Vessel disease (stenose > 70%), (%)				
One vessel	43.5	49.1	38.9	0.087
Multivessel	56.5	50.9	61.1	
Statines use (%)	62.6	52.6	47.4	0.109
TC (mmol/l)	4.3±1.4	4.3±1.3	4.4±1.6	0.743
TG (mmol/l)	1.7±1.3	1.5±1.2	1.8±1.4	0.053
HDL-c (mmol/l)	1.0±0.7	1.0±0.9	1.0±0.3	0.524
LDL-c (mmol/l)	2.6±1.4	2.6±1.4	2.6±1.3	0.968
ApoA-1 (g/l)	1.0±0.3	1.0±0.3	1.0±0.3	0.325
ApoB(g/l)	0.7±0.3	0.7±0.3	0.8±0.3	0.235
ApoB/ApoA-1	0.8±0.5	0.8±0.5	0.9±0.5	0.529
Lp(a) g/l)	0.2±0.3	0.2±0.2	0.2±0.3	0.129
Mediane	0.1	0.1	0.2	

DM: diabetes mellitus, **NDM:** non-diabetes mellitus**, BMI:** body mass index, **CAD:** coronary artery diseases, **LMCA:** Left main coronary artery, **LCx:** left circumflex, **LAD:** left anterior descending, **RCA:** right coronary artery. Values are expressed as the mean ± SD. P < 0.05.

The DM group had significant higher incidence of smoking, hypertension, dyslipidemia, obesity, and a lower rate of statin drugs use than the non-DM group. In all patients, 72.6 % on artery disease involved the left anterior descending (LAD) as the culprit vessel, 50.7 % the left circumflex (LCx),

48.4% the right coronary artery (RCA). 61.1% of DM patients had multivessel disease and 66.1% had severe stenose>70%.

Differences in lipidic profile and apolipoproteins between DM and NDM patients were evaluated. Mean TC, TG, LDL-c, HDL-c, apoA-1, apoB and ApoB/ApoA-1 ratio levels between these groups did not show significant differences. But, there was a marked increase in serum concentration levels of TC, TG, LDL-c, apoB and ApoB/ApoA-1 ratio in patients with high levels of ApoB/ApoA-1(>0.9). The highest levels were found in diabetic patients with high levels of ApoB/ApoA-1(>0.9) comparing to non-diabetic. In contrast, HDL-c and apoA-1 levels showed significant decrease in patients with high levels of ApoB/ApoA-1(>0.9). TC, LDL-c, TG, ApoB, ApoB/ApoA-1, HDL-c and apoA-1 levels were significantly different in these groups ($p<0.05$). Lipoprotein(a) levels didn't show significant difference between these groups (**Table 2**).

TABLE 2: BIOCHEMICAL CHARACTERISTICS IN DIABETIC AND NON-DIABETIC PATIENTS IN HIGH AND LOW GROUPS OF APO B/APOA-1 RATIO

Biochemical parameters	Low(<0.9)		High(>0.9)		P
	NDM	DM	NDM	DM	
Glucose (mmol/l)	7.0±2.5	13.1±6.6	7.4±3.8	12.5±7.1	0.991
HbA1c %	6.2±1.6	9.2±2.8	5.8±0.4	9.7±1.9	0.453
TC (mmol/l)	4.1±1.2	4.0±1.5	5.2±1.3	5.4±1.4	<0.001
TG (mmol/l)	1.4±0.7	1.6±1.0	1.9±2.2	2.0±0.9	0.013
Mediane	1.2	1.4	1.3	1.6	
HDL-c (mmol/l)	1.0±0.4	1.0±0.4	0.8±0.2	0.9±0.2	0.004
LDL-c (mmol/l)	2.4±1.2	2.3±1.2	3.5±1.0	3.6±1.4	<0.001
ApoA-1 (g/l)	1.0±0.2	1.1±0.3	0.9±0.2	0.8±0.3	<0.001
ApoB (g/l)	0.6±0.2	0.6±0.2	1.0±0.3	1.0±0.3	<0.001
ApoB/ApoA-1	0.6±0.2	0.6±0.2	1.3±0.8	1.3±0.5	<0.001
Lp(a) (g/l)	0.2±0.2	0.2±0.2	0.1±0.1	0.2±0.4	0.570
Mediane	0.1	0.6	0.1	0.1	

DM: diabetes mellitus, **NDM:** non-diabetes mellitus, **HbA1c:** glycosylated hemoglobin A1C, **TC:** total cholesterol, **TG:** triglycerides, **HDL-c:** high density lipoprotein cholesterol, **LDL-c:** low density lipoprotein cholesterol, **ApoA-1:** apolipoprotein A-1, **ApoB:** apolipoprotein B, **Lp(a):** Lipoprotein(a). Values are expressed as the mean ± SD. $P < 0.05$.

The DM group had significantly higher levels of TC, LDL-c, TG, ApoB and apoB/apoA-1 ratio in patients with high levels of apoB/apoA-1 but no significant differences in Lp(a). The highest levels were not shown in only patients with multivessel disease. ApoA-1 and HDL-c had significantly higher levels in patients with low levels of apoB/apoA-1 (**Table 3**).

TABLE 3: BIOCHEMICAL CHARACTERISTICS IN DIABETIC AND NON-DIABETIC PATIENTS CATEGORIZED ACCORDING TO VESSEL DISEASE

Biochemical parameters	Low (<0.9)				High (>0.9)				P
	One Vessel		Multi Vessel		One Vessel		Multi Vessel		
	NDM	DM	NDM	DM	NDM	DM	NDM	DM	
TC (mmol/l)	4.1±1.1	3.8±1.4	3.9±1.1	3.9±1.2	5.5±1.4	6.0±1.3	5.0±1.2	5.2±1.3	<0.001
HDL-c (mmol/l)	1.0±0.3	1.1±0.5	1.0±0.5	0.9±0.4	0.7±0.2	0.9±0.3	0.8±0.3	0.9±0.3	0.013
LDL-c (mmol/l)	3.5±0.9	2.1±1.2	2.3±1.1	2.4±0.8	3.7±1.0	4.4±1.3	3.4±1.0	3.3±1.3	<0.001
TG (mmol/l)	1.2±0.6	1.5±1.3	1.4±0.7	1.5±0.8	2.3±3.1	1.6±0.6	1.6±0.6	2.2±1.0	0.007
Mediane	1.2	1.2	1.2	1.4	1.3	1.5	1.3	2.0	
ApoA-1 (g/l)	1.0±0.2	1.1±0.2	0.9±0.2	1.0±0.2	0.8±0.3	0.9±0.2	0.9±0.2	0.8±0.3	<0.001
ApoB (g/l)	0.6±0.1	0.6±0.2	0.6±0.1	0.6±0.2	0.9±0.3	1.0±0.3	1.0±0.2	1.0±0.2	<0.001
ApoB/ApoA-1	0.6±0.2	0.5±0.2	0.6±0.1	0.6±0.2	1.4±1.1	1.2±0.2	1.1±0.2	1.4±0.6	<0.001
Lp(a) (g/l)	0.1±0.2	0.2±0.2	0.1±0.2	0.2±0.1	0.1±0.1	0.4±0.1	0.1±0.1	0.2±0.1	0.837
Mediane	0.1	0.1	0.1	0.2	0.1	0.2	0.1	0.1	

DM: diabetes mellitus, **NDM:** non-diabetes mellitus, **TC:** total cholesterol, **TG:** triglycerides, **HDL-c:** high density lipoprotein cholesterol, **LDL-c:** low density lipoprotein cholesterol, **ApoA-1:** apolipoprotein A-1, **ApoB:** apolipoprotein B, **Lp(a):** Lipoprotein(a). Values are expressed as the mean ± SD. $P < 0.05$.

The serum concentration levels of apoB/apoA-1 ratio, apolipoproteins and lipidic profile components in patients with significant stenosis (>50%) were more elevated than patients with mild stenosis (<50%) and the difference intergroups were significant (p<0.05) (**Table 4).**

ROC Curve for ApoB/ApoA-1 ratio in predicting CAD in T2DM: The area under the ROC curve for ApoB/ApoA-1 in patients with T2DM was (0.513±0.041 (95% CI: 0.443, 0.594), p=0.749; ApoB/ApoA-1 don't display significant value in predicting severity in CAD patients with T2DM (**Fig. 1**).

TABLE 4: BIOCHEMICAL CHARACTERISTICS IN DIABETIC AND NON-DIABETIC PATIENTS WITH SIGNIFICANT STENOSIS

Biochemical parameters	Low(<0.9)				High(>0.9)				P
	Stenose [50-70]%		Stenose >70 %		Stenose [50-70]%		Stenose >70 %		
	NDM	DM	NDM	DM	NDM	DM	NDM	DM	
CT (mmol/l)	3.5±1.0	4.1±1.4	4.4±1.1	3.8±1.2	5.0±1.4	5.7±1.3	5.6±0.7	5.4±0.9	<0.001
HDLc (mmol/l)	1.0±0.2	1.0±0.3	1.0±0.4	0.8±0.3	0.9±0.6	1.2±0.2	0.9±0.3	0.9±0.2	0.863
LDLc (mmol/l)	1.8±0.9	2.6±1.5	2.8±0.9	2.3±0.8	3.1±1.5	3.3±1.1	3.8±0.5	3.7±0.8	<0.001
TG (mmol/l)	1.4±0.9	1.4±0.7	1.2±0.5	1.6±1.2	2.2±1.5	2.7±1.1	1.8±0.5	2.0±0.9	0.004
ApoA-1 (g/l)	1.0±0.3	1.1±0.2	1.0±0.1	0.9±0.2	0.7±0.2	1.0±0.2	1.0±0.1	0.8±0.2	0.022
ApoB (g/l)	0.5±0.2	0.8±0.3	0.7±0.1	0.6±0.2	0.8±0.1	1.1±0.2	1.1±0.3	1.0±0.3	<0.001
ApoB/ApoA-1	0.6±0.3	0.7±0.1	0.7±0.1	0.6±0.2	1.3±0.3	1.1±0.1	1.1±0.2	1.4±0.6	<0.001
Lp(a) (g/l)	0.1±0.1	0.1±0.1	0.2±0.2	0.2±0.2	0.1±0.1	0.2±0.2	0.1±0.1	0.1±0.2	0.296
Mediane	0.1	0.1	0.1	0.2	0.1	0.1	0.1	0.1	

DM: diabetes mellitus, **NDM:** non-diabetes mellitus, **TC:** total cholesterol, **TG:** triglycerides, **HDL-c:** high density lipoprotein cholesterol, **LDL-c:** low density lipoprotein cholesterol, **ApoA-1:** apolipoprotein A-1, **ApoB:** apolipoprotein B, **Lp(a):** Lipoprotein(a). Values are expressed as the mean ± SD. P < 0.05.

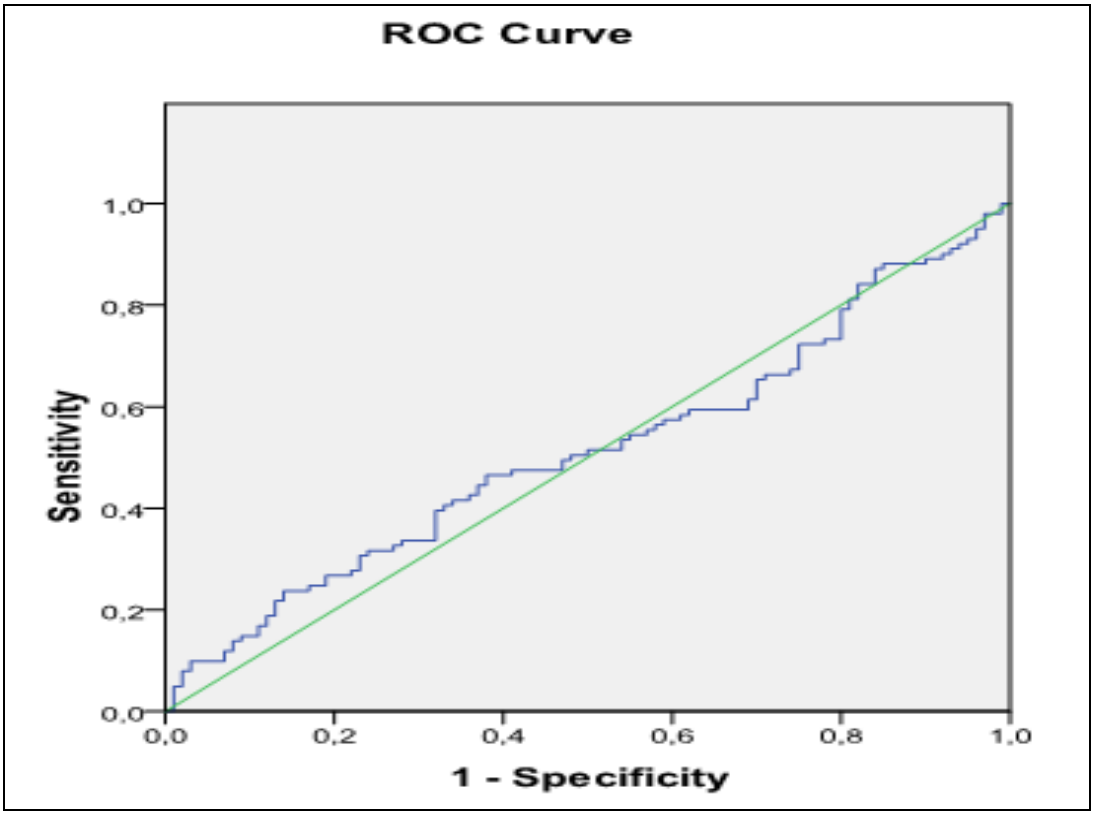

FIG. 1: RECEIVER-OPERATING CHARACTERISTIC (ROC) CURVE FOR APOB/APOA1 IN PREDICTING CORONARY ARTERY DISEASE IN PATIENTS WITH T2DM.

Area under the receiver-operating characteristic curve: ApoB/ApoA1: 0.513±0.041 (95% CI: 0.443, 0.594), p=0.749; ApoB/ApoA-1 don't display significant value in predicting severity in CAD patients with T2DM.

DISCUSSION: In this study, it was particularly evident that the baseline lipid and lipoprotein profiles were significantly higher in diabetic patients with high levels of the ratio ApoB/ApoA-1 than those with low levels of this ratio. In addition, our results show that the study of high level of the ApoB/ApoA-1 ratio seems to be better correlated with the severity of CAD as defined by the observation of vessel diseases and the degree of stenosis in patients with DM than total ApoB/ApoA-1 ratio. As shown in ROC curve, the fact that the serum levels of the ratio ApoB/ApoA-1 are not clearly predictive in T2DM in CAD patients, and the absence of significant differences in the degree of stenosis and vessel disease between diabetic and non diabetic patients as shown in table 1, could be due to other CAD risk factors such as blood pressure, smoking, obesity, and the use of lipidic lowring drugs.

In fact, the apoB/apoA-1 ratio which reflects the risk due to proatherogenic and antiatherogenic lipoproteins [11], is a well-established biomarker for the development of atherosclerotic disorders as well as adverse cardiovascular diseases outcome [12]. These findings were shown in some previous studies, in the Apoprotein-related Mortality Risk (AMORIS) cohort conducted in 94,667 men and 75,675 women, the ratio of TC/HDL-C and apoB/apoA-1 were directly compared to estimate the lipoprotein-related risk of vascular disease. The authors concluded that the apoB/apoA-1 ratio, both in men and women, was better than any of the conventional lipid ratios in these settings [13].

In the United States population, apoB/apoA-1 ratio was significantly associated with insulin resistance in non-diabetic subjects, independently of the traditional risk factors, metabolic syndrome components, and inflammatory risk factors [14]. Also, in a Chinese study performed on diabetics with stable angina pectoris the higher ratios of apoB/apoA-1 were associated with, more severe the CAD would be when assessed with Gensini scores. A case in point is the evidence from Indian diabetic patients which suggested that the ratio of apoB and apoA-1 provided better information regarding the risk of CAD in diabetic patients [13]. Another study indicated that the apoB/apoA-1 ratio was significantly associated with insulin resistance in non-diabetic subjects, independent of other risk factors [15].

Sierra-Johnson and al. [14] support the notion that lipoprotein abnormalities that are part of the metabolic-risk-factor clustering are significantly associated with insulin resistance and that they may provide additional mechanistic information on the complex metabolic syndrome. Thereby, the apoB/apoA-1 ratio is strongly associated with insulin resistance beyond the association explained by traditional risk factors, metabolic syndrome components, and inflammatory risk factors. Their findings were be explained by the fact that the basis for the metabolic-risk-factor clustering concept is that insulin resistance is the primary underlying pathophysiological disturbance that clusters along with atherogenic dyslipidaemia, elevated blood pressure, elevated plasma glucose, a prothrombotic state, and a proinflammatory state that ultimately may lead to increase cardiovascular risk [14].

According to our results, it is tempting to hypothesis that abnormalities in the lipid profiles, apolipoproteins and lipoprotein might account for the increased risk for development of type 2 diabetes. In fact, a possible explanation for the positive association between the apoB/apoA-1 ratio and the severity of CAD could be explained that apolipoproteins regulate the synthesis and metabolism of lipoprotein particles and in addition stabilize their structure. These lipoprotein particles are composed of phospholipids, free cholesterol, triglycerides, cholesterol esters, and apolipoprotein molecules [14]. Oxidation of lipoproteins involves the attack on many constituents, including cholesterol, fatty acids, antioxidants and apoB [16].

The association of apoB with incident T2DM has been proven with improved risk prediction compared to LDL-c or HDL-c [17]. Increased glycation of apoB corroborated with the finding that the presence of small dense LDL with persistent hyperglycemia increases susceptibility of LDL to undergo glycation. The presence of plaques and increased thickness of intima indicates that glycated apoB predisposes diabetics to atherosclerosis [18]. High ApoA-1 levels independently predicted incident type-2 diabetes among a sample of Turkish participants and the top tertile of serum ApoA-1 level nearly doubled the

risk for incident diabetes when compared with the low tertile. Beneficial HDL can be degenerated to a dysfunctional HDL with pro-atherosclerotic and pro-inflammatory properties using oxidation and glycation [17]. HDLs and apoA-1 increase insulin synthesis and secretion in pancreatic β cells [19].

In pre-diabetic patients, reduced HDL-c has been reported to be associated with progression to T2DM [17]. Elevated plasma LDL-c and triacylglycerol, and reduced HDL-cholesterol contribute to accelerate atherogenesis in T2DM [20]. LDLs modify the antithrombotic properties of the vascular endothelium and change vessel contractility by reducing the availability of endothelial nitric oxide and activating proinflammatory signaling pathways. LDL entering affected vessels undergo modifications including glycation and conversion to small dense form. These modifications potentiate its atherogenic properties [18]. The formation of small dense LDL is closely associated with insulin resistance and hypertriglyceridemia. However, small dense LDL was also observed in patients with type 2 diabetes and insulin resistance with close to normal triglyceride levels. This might be explained by increased hepatic lipase activity commonly seen in patients with type 2 diabetes [21].

Lp(a), another lipoprotein, is a form of LDL that is modified in the liver by covalent attachment of apoB to apoA-1 [16]. In addition, LDL and Lp(a) are retained in the arterial intima and is modified by the intimal enzymes and agents. Lp(a) is rich in potentially atherogenic oxidized phospholipids. Lp(a) also has antifibrinolytic effects, which enhance its atherogenicity [16]. Although its importance in lesion development, our results don't show significant difference in Lp(a). This can be explained by the fact that majority of the study patients has been receiving lipid-lowering agents. It has been shown that LDL-lowering drugs are the most effective therapy against atherothrombotic cardiovascular disease and decrease the probability that apoB-containing lipoproteins will be retained in the subendothelium [16].

In our study, although high levels of apoB/apoA-1 (>0.9) were associated with the presence and the severity of CAD, the AUC (AUC=0.513, P=0.749) following the ROC analysis falls into the range [0.443-0.594], which indicates that apoB/apoA-1 was a low predictive marker, and the cut-off value of 0.9 cannot be categorized as an ideal value to identify the severity of CAD effectively in T2DM. Nevertheless, the addition of the apoB/apoA-1 ratio may compensate for the inadequacy of other lipidic profiles and apolipoproteins alone and may be a valuable tool in the atherogen risk assessment of diabetic patients and the severity of coronary stenosis.

There are some limitations to our study that deserve. We should compare the usefulness ApoB/ApoA-1 ratio for predicting the severity of CAD in diabetic patients without other cardiovascular risk factor as dyslipidemia, which need lipid-lowering drugs. Moreover, as sample size is limited, the current study population might be unable to represent diabetic Tunisian population.

CONCLUSION: The apoB/apoA-1 ratio is not associated with the severity of CAD in patients with T2DM in contrast to its high levels which might be contributed to the assessment of patients at high cardiovascular risk.

CONFLICT OF INTERESTS: The authors declare that they have no competing interests.

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