

## *Original Research Article*

# **Lipoprotein-associated Phospholipase A<sub>2</sub> Activity Contributes to the Coronary Artery Disease with Metabolic Syndrome**

**Comment [U1]:** Topic can be better presented to bring out a better perception of the study

**Running title:** LP A<sub>2</sub> activity is a risk for the coronary artery disease with metabolic Syndrome

**Comment [U2]:** Should be reframe and include in discussion as a prime study concept

### **ABSTRACT**

**Objective:** The aim is to determine contribution of Lp-PLA<sub>2</sub> to coronary artery disease (CA) in patients with and without Metabolic Syndrome (MetSynd).

**Comment [U3]:** 1. Abstract should have a brief overview of the introduction, objectives, methods --- down to conclusion but doesn't have to be segregated (no sub-title in abstract)

**Subjects and methods:** This is a cohort prospective study based on 412 patients male and female who were eligible and aged 25-75 years old patients and gave consent to participate in study. The study included socio-demographics, clinical biochemistry and the presence of co-morbid diseases. The data were analyzed using descriptive and multivariate analyses.

**Comment [U4]:** Reframe, as abstract is supposed to start with an introduction of the research concept

**Results:** There was a significant difference between MetSynd Positive versus MetSynd Negative with respect to age groups, gender, BMI, smoking, nargile use, thyroid, COPD, CAD, hypertension, diabetes, and stroke. Also, there was a significant difference between MetSynd Positive versus

**Comment [U5]:** Have to fully define MetSynd as it is the first mentioning

**Comment [U6]:** Avoid using abbreviations, when mentioning a term for the first time

MetSynd Negative with respect to BMI, Waist Circumference, hemoglobin, HbA1c, vitamin B12, fasting blood glucose (mmol/L), vitamin D (mmol/L), calcium (mmol/L), creatinine (mg/dL), triglyceride (mmol/L), uric acid (mmol/L), ferritin (mmol/L), systolic BP (mm Hg) and diastolic BP (mm Hg), creatine kinase-myocardial band (CK-MB); (ug/L)(p=0.001); Lp-PLA<sub>2</sub> activity, nmol/min/ml, (p=0.001); HOMA-IR index, (p=0.004), Insulin (μIU/dl) (p=0.001); C-reactive protein (mg/L) (p=0.004); White blood cell (/mm<sup>3</sup>)(p=0.008); Platelet (10<sup>3</sup>/mm<sup>3</sup>)(p= 0.018) Mean Plate Volume (mg/L) (p= 0.032); red cell distribution width (mg/L) (p=0.001); and vitamin D levels (p=0.018), respectively. The study confirmed correlations between the MetSynd and clinical biochemical parameters including: Body Mass Index-BMI (kg/m<sup>2</sup>) (r= -0.117); uric acid (r=-0.131); ferritin (r=0.164,); systolic BP (r= -0.141); diastolic BP (r=-0.255); CK-MB (r=-0.164); Lp-PLA<sub>2</sub> (r=-0.166); HOMA-Insulin Resistance (r=-0.142); Mean Plate Volume (r=0.106,); Platelet (r=0.117); RDW (r=0.185); WBC (r=0.130); vitamin D level (r= 0.141); HbA1c (%) (r=-0.123); vitamin B12 (r= 0.11916); and calcium (r= 0.175) respectively. The multivariate stepwise regression analysis indicated that Lp-PLA<sub>2</sub> nmol/min/ml (p<0.001), BMI (kg/m<sup>2</sup>) (p<0.001), systolic BP (p<0.001), MetSynd (p=0.002), CK-MB (p=0.019), Calcium (mmol/L) (p= 0.023), Triglyceride (mmol/L) (p=

0.029), Total-cholesterol (mmol/L) ( $p=0.046$ ) were considered as risk predictors of the CAD patients after adjusting for age and gender.

**Conclusion:** the present analysis is the first one studying the contribution of Lp-LPA2 to CAD in the presence of MetSynd, and these findings indicate that Lp-PLA2 may play a role in the process of CAD regarding MetSynd.

**Comment [U7]:** Abstract spacing should be one line spacing

**Key words:** Lipoprotein-associated Phospholipase, A<sub>2</sub> Activity, Coronary Artery Disease, Metabolic Syndrome

## Introduction

**Comment [U8]:** Presentation of the introductory part can be improved

Coronary Artery disease (CAD) is a pathological inflammatory process characterized by atherosclerotic accumulation in the epicardial arteries. It has been known for more than half a century that the risk factors for CAD include hypertension, increased levels of low-density lipoprotein cholesterol (LDL-C), type-2 diabetes and smoking. The MetSynd is a cluster of the most dangerous risk factors for the coronary artery disease (CA), CHD, stroke, diabetes or prediabetes, abdominal obesity, changes in cholesterol and high blood pressure [1-6].

**Comment [U10]:** Citations can be from one or two references

Inflammation has been increasingly recognised as a critical step in the pathogenesis of coronary artery disease (CAD) and MetSynd [5-9]. Lipoprotein-associated phospholipase A<sub>2</sub> (Lp-PLA<sub>2</sub>) is a novel inflammatory marker associated with MetS, low density lipoprotein (LDL) cholesterol, atherosclerotic disease and incident cardiovascular disease (CVD). Lp-PLA<sub>2</sub> has a role of proatherogenic, and determines risk factor for CVD events [10-13]. To the best of our knowledge, it is unclear whether Lp-PLA<sub>2</sub> would contribute to CAD in case of MetSyn. CAD is the most leading cause of mortality and morbidity worldwide. The aim of current study was to investigate the possible contribution of Lp-PLA<sub>2</sub> to coronary artery disease in patients with and without MetSynd.

**Comment [U11]:** Remove the space

## Subjects and Methods

**Comment [U12]:** Reframe to Methodology

The current study based on cohort design a total of 412 patients and aged from 25 to 75 years, cardiology outpatient's were reviewed from January 2019 to November 2021. Patients' demographic, clinical and laboratory data were collected from the hospital. Waist circumference was measured at the level of superior iliac crest, Systolic and diastolic BP was measured in the patient's right arm with a mercury sphygmomanometer.

The study was performed according to the principles of 1975 Declaration of Helsinki and its subsequent revisions. The study protocol was approved by the XXXX University clinical research ethic committee [Ethics Committee Decision No; 2/2021.K-78) (IRB# 10840098-604.01.01-E and IRB# 10840098-604.01.01-E.8421). Informed consent was obtained from the all patients.

**Comment [U13]:** Delete double spacing

**Comment [U14]:** Is this the corrected name of the committee

#### **Lp-PLA2 activity assay**

**Comment [U15]:** Sub-title should be sentence case

The total plasma Lp-PLA2 activity was measured using an enzyme immunoassay (EIA) kit. LDL-C, HDL-C, HBA1C, TC, TG and FPG levels were measured using colorimetric method. Serum insulin levels were determined by an enzymatic method using A. Insulin resistance was assessed by the homeostasis model assessment equation (HOMA-IR) [15].

#### **Definition of metabolic syndrome**

In our study, MetSynd was defined according to the diagnostic criteria recommended by the Society of Endocrinology and Metabolism of Turkey in accordance with the recommendation of the World Health Organisation (WHO) [6-7] at least one of the following criteria of insulin resistance [1 and impaired impaired FPG  $\geq 110$  mg/dL, impaired PG tolerance (2h PG  $\geq 140$  mg/dL) elevated insulin levels (4th quartile of reference). Plus two or more of the following: Systolic BP  $\geq 140$  mm Hg and/or, diastolic BP  $\geq 90$  mm Hg; [18]; TG  $\geq 150$  mg/dL, and/or HDL-C  $< 35$  mg/dL for men and  $< 40$  mg/dL for women. Central obesity: waist/hip ratio  $> 0.90$  for men and  $0.85$  for women and/or BMI  $> 30$  kg/m<sup>2</sup> diagnosed hypertension Microalbuminuria: Urinary albumin excretion rate  $\geq 20$  mg/ml or albumin/creatinine ratio  $\geq 30$  mg/g

**Comment [U16]:** Reframe e.g 16 and 17 or 16/17

#### **Coronary Computed Tomography Angiography (CCTA)**

Patients were scanned with a 412-slice CT-scanner [19-20] (Philips, Holland) using prospective cohort scanning techniques. All patient's vital signs were monitored during CCTA. Patients received a beta-blocked (50-100 mg oral Metoprolol) one hour prior to scanning if their heart rate was upper than 65 beat/min. The CCTA analysis [19-20]. was performed by an experinced observers blinded to the study. CAD was defined as the occurrence of a visible plaque in at least 1 of 15 coronary segments according to guidelines.

#### **Statistical analysis**

Student-t test and. Chi-square test weres used to test for between groups. The Pearson correlation analysis was performed between two continuous variables. Multivariate stepwise regression analysis method was used to predict risk factors for the CAD. The level  $p < 0.05$  was considered as the cut-off value for significance.

**Comment [U17]:** Reframe and remove the s

## Results

**Comment [U18]:** Presentation of results is quite very poor and must be improved and presents results in to real scientific tables

Table 1 shows socio-demographic characteristics of subjects COVID-19 by Metabolic Syndrome. There was a significant difference between Metabolic Syndrome Positive versus Metabolic Syndrome Negative with respect to age groups, gender, BMI, smoking cigarette, nargile use, thyroid, COPD, Coronary Artery Disease (CAD), hypertension, diabetic and stroke.

**Comment [U19]:** Delete space

Table 2 presents the baseline values of biochemistry indices by metabolic syndrome patients. There was a significant difference between Metabolic Syndrome Positive versus Metabolic Syndrome Negative with respect to BMI, Waist Circumference, hemoglobin, HbA1c, vitamin B12, fasting blood glucose (mmol/L), vitamin D (mmol/L), calcium (mmol/L), creatinine (mg/dL), triglyceride (mmol/L), uric acid (mmol/L), ferritin (mmol/L), systolic BP (mm Hg) and diastolic Bp (mm Hg), respectively.

Table 3 gives the clinical biochemical values by metabolic syndrome patients. There was a significant difference between Metabolic Syndrome Positive versus Metabolic Syndrome Negative including: creatine kinase-myocardial band; (ug/L)(p=0.001); Lp-PLA2 activity, nmol/min/ML, (p=0.001); HOMA-IR index,(p=0.004), Insulin ( $\mu$ IU/dl) (p=0.001); C-reactive protein (mg/L) (p=0.004); White blood cell (/mm<sup>3</sup>)(p=0.008); Platelet (10<sup>3</sup>/mm<sup>3</sup>)(p= 0.018) Mean Plate Volume (mg/L) (p= 0.032); red cell distribution width (mg/L) (p=0.001); and vitamin D levels (p=0.018), respectively.

Table 4 presents the correlations between the metabolic syndrome and clinical biochemical parameters including: Body Mass Index-BMI (kg/m<sup>2</sup>) (r= -0.117, p=0.018);Uric acid (r=-0.131, p=0.008); ferritin (r=0.164, p=0.001); systolic BP (r= -0.141, p=0.004); diastolic BP (r=-0.255, p=0.001); CK-MB (r=-0.164, p=0.001); Lipoprotein-associated Phospholipase A2(r=-0.166, p=0.001); HOMA-Insulin Resistance (r=-0.142, p=0.004); Mean Plate Volume (r=0.106, p=0.032); Platelet (r=0.117, p=0.018); Red cell distribution width (r=0.185, p=0.001); White Blood Count (r=0.130, p=0.008); vitamin D level (r= 0.141, p=0.012); Hemoglobin A1c (%) (r=-0.123, p=0.004); vitamin B12 (r= 0.119, p=0.016); and calcium (r= 0.175, p=0.004) respectively.

Table 5 shows the relationship and risk predictors of the Coronary Artery Disease patients using multivariate stepwise regression analysis method. The multivariate stepwise regression analysis indicated that Lipoprotein-associated Phospholipase A2 nmol/min/ML (p<0.001), Body Mass Index (kg/m<sup>2</sup>) (p<0.001), systolic blood pressure (p<0.001), metabolic syndrome ATP III (p=0.002), Creatine kinase myocardial band (p=0.019), Calcium (mmol/L) (p= 0.023), Triglyceride

(mmol/L) ( $p=0.029$ ), Total cholesterol (mmol/L) ( $p=0.046$ ) were considered as risk predictors of the CAD patients after adjusting for age and gender.

**Comment [U20]:** Results should be presented in tables as stated

## Discussion:

This study identified increased total plasma Lp-PLA2 activity in patients with the metabolic Syndrome, especially in those with coronary artery disease when compared to the patients without metabolic syndrome. To point out, our data provided that elevated Lp-PLA2 activity indicates increased risk of CAD with Metabolic syndrome.

**Comment [U21]:** Delete space and correct other subsequent paragraphs

The current study revealed that Lp-PLA2 activity was significantly higher in subjects with Metabolic Syndrome in our study. These findings are similar to those from the Bruneck Study [3]. In the current study we have achieved significant associations between metabolic syndrome ATP III and Body Mass Index (kg/m<sup>2</sup>), uric acid (mmol/L), ferritin (ug/L), systolic BP mm Hg, diastolic BP mm Hg, CK-MB (ug/L), HOMA-Insulin Resistance, Mean Plate Volume (mg/L), platelet (mg/L), red cell distribution width (mg/L), White Blood Count-WBC (/mm<sup>3</sup>), vitamin D (ng/ml), hemoglobin A1c (%), vitamin B12, and calcium (mmol/L). Those results are consistent with Tsimikas et al. [3]. Additionally, this study confirms the strong association between Lp-PLA2 levels and the metabolic syndrome [2, 7].

**Comment [U22]:** Reframe

**Comment [U23]:** Should be italicize

The Malmö Study findings are consistent with a recent report from the Intermountain Heart Collaborative Study [9], where 42% had the metabolic syndrome. There is observational evidence that Lp-PLA2 may be a useful guide for therapeutic efficacy [21-23]. Lp-PLA2 is complementary to CRP for risk assessment in patients with MetSynd [22-23]. The current results confirmed the hypothesis that Lp-PLA2 may be a potential risk marker for CAD in the Turkish population. Further, a total of 429 patients in German population with suspected acute coronary syndrome were analysed and Lp-PLA2 turned out to be a more effective risk marker than high sensitivity CRP in these patients. The above different population studies are consistent and confirmed our present study.

Furthermore, Persson et al [7] explored to investigate the role of lipoprotein associated phospholipase A2 (Lp-PLA2) with the MetSynd, and incident cardiovascular disease (CVD) among Swedish patients. The study results revealed that the cohort study of Lp-PLA2 is associated with the MetS. There is an excellent agreement between Persson et al [7] Sweden study and current study.

**Comment [U24]:** Reframe and cite correctly

In most recent conducted study [25] that use of postmenopausal hormones, not smoking, and having a BMI less than 25 kg/m<sup>2</sup> where favorably confer a beneficial effect on Lp-PLA2 activity.

Therefore, Lp-PLA2 activity may represent a novel pathway correlated with increased CAD. Overall, this results are similar and confirmative with our current results outcome.

To the best of our knowledge, the present analysis is the first one studying the contribution of Lp-LPA2 to CAD in the presence of MetSynd, and these findings indicate that Lp-PLA2 may play a role in the process of CAD independently of MetSynd. As well as, we used locally recommendation regarding waist circumference measurement for the diagnosis of MetSynd.

**Comment [U25]:** Statement can be better represented and should be subjective not objective

#### **limitations:**

The present study have several limitations. Firstly, the study based on a single measurements of plasma Lp-PLA2. Secondly, we were unable to rule out the possible impact of aspirin, beta blockers, statins and fibric acid derivatives on Lp-PLA2 activity in the current findings, as reports. Thirdly, the study was conducted within the outpatient patients registered in cardiology clinics. The study was conducted as a two-center study that includes different groups of critically patients. This fact limits the generalizability of the results and establishes a need for multicentre international studies to achieve a better understanding of such outcome predictors.

#### **Conclusion:**

The present analysis is the first one studying the contribution of Lp-LPA2 to CAD in the presence of MetSynd, and these findings indicate that Lp-PLA2 playing a great role in the process of CAD regarding MetSynd.

**Ethics Committee Approval:** The authors would like to thank the Istanbul Medipol University for their support and the Clinical Research Ethics Committee of Istanbul Medipol University, Institutional Review Board. Also The study protocol was approved by the Istinye University clinical research ethic committee Ethics Committee Decision No. were 2/2021.K-78) (IRB# 10840098-604.01.01-E.3193 and IRB# 10840098-604.01.01-E.8421). Informed consent were obtained from the all patients

**Comment [U26]:** Reframe and should be remove as ethical approval is not an acknowledgement

#### **REFERENCES:**

**Comment [U27]:** All the listed references should be reframe following the same and accepted format and check out individual rules of referencing

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**Table 1. Socio-demographic characteristics of patients by metabolic syndrome (N = 412)****Comment [U28]:** This representation should be in the result section

Variables	Metabolic Syndrome Positive n = 126 (%)	Metabolic Syndrome Negative n = 286 (%)	p-value Significance
<b>Age group</b>			
<40	34 (27.0)	82 (28.7)	
40-49	34 (27.0)	45 (15.7)	<b>0.025</b>
=>50	58 (46.0)	159 (55.6)	
<b>Gender</b>			
Male	89 (70.6)	150 (52.4)	<b>0.001</b>
Female	37 (29.4)	136 (47.6)	
<b>BMI (25 kg/m<sup>2</sup>)</b>			
Normal (<25 kg/m <sup>2</sup> )	25 (19.8)	91 (40.9)	
Overweight (29-30 kg/m <sup>2</sup> )	57 (45.2)	117 (27.3)	<b>0.037</b>
Obese (>30 kg/m <sup>2</sup> )	44 (34.9)	78 (30.1)	
<b>Cigarette Smoke</b>			
Yes	35 (27.8)	49 (17.1)	<b>0.013</b>
No	91 (72.2)	237 (82.9)	
<b>Nargile-smoking</b>			
Yes	21 (16.7)	24 (8.4)	<b>0.012</b>
No	105 (83.3)	262 (91.6)	
<b>Diabetes</b>			
Yes	27 (21.4)	30 (10.5)	<b>0.003</b>
No	99 (78.6)	256 (89.5)	
<b>Thyroid</b>			
Yes	38 (30.2)	113 (24.6)	<b>0.002</b>
No	88 (69.8)	346 (75.4)	
<b>Chronic Obstructive Pulmonary Disease</b>			
Yes	30 (23.8)	37 (12.9)	<b>0.005</b>
No	96 (76.2)	249 (87.1)	
<b>Hypertension</b>			
Yes	43 (34.1)	64 (22.4)	<b>0.009</b>
No	83 (65.9)	222 (73.6)	
<b>Coronary Artery Disease</b>			
Yes	65 (51.6)	103 (36.0)	<b>0.003</b>
No	61 (48.4)	183 (84.0)	
<b>Stroke</b>			
Yes	32 (25.4)	91 (31.8)	0.201
No	94 (74.6)	195 (68.2)	
<b>Coronary Heart Failure</b>			
Yes	43 (34.1)	69 (24.1)	
No	83 (65.9)	217 (75.9)	<b>0.025</b>

**Table 2. Clinical biochemistry base data values by metabolic syndrome patients (N= 412)**

<b>Variables</b>	<b>Metabolic Syndrome Positive = 126 Mean <math>\pm</math> SD</b>	<b>Metabolic Syndrome Negative = 286 Mean <math>\pm</math> SD</b>	<b>P value</b>
BMI kg/m <sup>2</sup>	28.52 $\pm$ 4.48	27.04 $\pm$ 4.36	<b>0.018</b>
Waist Circumference, cm	104.35 $\pm$ 8.34	97.55 $\pm$ 11.95	<b>0.001</b>
Hemoglobin (g/dL)	11.92 $\pm$ 2.77	12.66 $\pm$ 2.57	<b>0.009</b>
HbA1c	5.96 $\pm$ 0.91	5.74 $\pm$ 0.77	<b>0.012</b>
Fasting Blood Glucose (mmol/L)	111.91 $\pm$ 45.01	103.07 $\pm$ 36.10	<b>0.050</b>
Vitamin D (mmol/L)	17.29 $\pm$ 7.17	19.47 $\pm$ 7.56	<b>0.006</b>
Vitamin B12	271.10 $\pm$ 125.0	300.8 $\pm$ 108.0	<b>0.016</b>
Calcium (mmol/L)	8.39 $\pm$ 0.77	8.86 $\pm$ 0.67	<b>0.001</b>
Urea (mg/dL)	53.95 $\pm$ 5.11	55.60 $\pm$ 4.56	0.738
Creatinine (mg/dL)	0.74 $\pm$ 0.16	0.69 $\pm$ 0.14	<b>0.001</b>
Albumin (mg/dL)	3.44 $\pm$ 0.64	3.43 $\pm$ 0.58	0.930
Total cholesterol (mmol/L)	193.5 $\pm$ 60.40	188.1 $\pm$ 56.8	0.386
HDL (mmol/L)	166.5 $\pm$ 83.9	203.0 $\pm$ 91.6	0.070
LDL (mmol/L)	122.0 $\pm$ 44.8	131.0 $\pm$ 86.7	0.276
Triglyceride (mmol/L)	172.94 $\pm$ 81.57	150.16 $\pm$ 95.63	<b>0.024</b>
Uric Acid (mmol/L)	6.56 $\pm$ 2.31	6.00 $\pm$ 1.77	<b>0.008</b>
Ferritin (ug/L)	133.62 $\pm$ 92.10	191.28 $\pm$ 80.71	<b>0.001</b>
TSH	1.57 $\pm$ 1.12	1.74 $\pm$ 1.15	0.151
Systolic Blood Pressure mm Hg	135.82 $\pm$ 10.00	133.10 $\pm$ 9.18	<b>0.004</b>
Diastolic Blood Pressure mm Hg	81.40 $\pm$ 6.28	78.00 $\pm$ 6.55	<b>0.001</b>

**Table 3. Clinical biochemistry baseline value by metabolic syndrome patients (N= 412)patients**

Variables	Metabolic Syndrome Positive = 126 Mean $\pm$ SD	Metabolic Syndrome Negative = 286 Mean $\pm$ SD	p value
Creatine kinase (ug/L)	40.47 $\pm$ 23.71	38.54 $\pm$ 20.55	0.403
Creatine kinase-myocardial band; (ug/L)	15.21 $\pm$ 8.96	12.74 $\pm$ 5.66	<b>0.001</b>
Lp-PLA2 activity (mmol/min/L)	647.92 $\pm$ 153.50	593.90 $\pm$ 146.27	<b>0.001</b>
HOMA-IR index	2.80 $\pm$ 1.63	2.30 $\pm$ 1.59	<b>0.004</b>
Insulin ( $\mu$ IU/dl)	11.31 $\pm$ 3.88	10.41 $\pm$ 4.27	<b>0.001</b>
C-reactive protein (mg/L)	13.56 $\pm$ 5.01	11.92 $\pm$ 7.42	<b>0.004</b>
White blood cell (/mm3)	7455.63 $\pm$ 1715.00	7906.3 $\pm$ 1495.25	<b>0.008</b>
Neutrophil (/mm3)	5.435 $\pm$ 3.02	5.44 $\pm$ 3.17	0.952
Lymphocyte (/mm3)	1.93 $\pm$ 0.93	1.98 $\pm$ 0.96	0.587
Platelet (103/mm3)	243.31 $\pm$ 97.03	267.72 $\pm$ 95.57	<b>0.018</b>
Mean Plate Volume (mg/L)	9.77 $\pm$ 1.15	9.99 $\pm$ 0.82	<b>0.032</b>
Mean corpuscular volume (mg/L)	85.98 $\pm$ 7.84	88.8 $\pm$ 5.20	0.542
Red cell distribution width (mg/L)	13.48 $\pm$ 1.50	14.26 $\pm$ 2.06	<b>0.001</b>
Vitamin D 20 ( ng/ml)	n (%)	n (%)	
Deficiency <20 ng/ml	86 (68.3)	153 (53.5)	
Insufficiency 20 -30 ng/ml	27 (21.4)	93 (62.5)	<b>0.019</b>
Sufficiency>30 ng/ml	13(10.3)	40(14.0)	

**Table 4. The correlation between metabolic syndrome and risk predictors of the Coronary Artery Disease (N = 412)**

Variables	Metabolic.syndrome	p value
Body Mass Index (kg/m2)	$r = -0.117^*$	0.018
Uric acid (mmol/L)	$r = -0.131^{**}$	0.008
Ferritin (ug/L)	$r = 0.164^{**}$	0.001
Systolic Blood Pressured mm Hg	$r = -0.141^{**}$	0.004
Diastolic Blood Pressure mm Hg	$r = -0.255^{**}$	0.001
CK-MB (ug/L)	$r = -0.164^{**}$	0.001
Lp-PLA2 activity (mmol/min/L)	$r = -0.166^{**}$	0.001
HOMA-Insulin Resistance	$r = -0.142^{**}$	0.004
Mean Plate Volume (mg/L)	$r = 0.106^*$	0.032
Platelet (mg/L)	$r = 0.117^*$	0.018
Red cell distribution width (mg/L)	$r = 0.185^{**}$	0.001
White Blood Count (/mm3)	$r = 0.130^{**}$	0.008
Vitamin D ( ng/ml)	$r = 0.141^{**}$	0.004
Hemoglobin A1c (%)	$r = -0.123^*$	0.012
Vitamin B12	$r = 0.119^*$	0.016
Calcium (mmol/L)	$r = 0.175^{**}$	0.004

**Table 5. The relationship and risk predictors of the Coronary Artery Disease patients using multivariate stepwise regression analysis (N=412).**

Variables	Regression coefficient	Standard Error	St. Coefficients Beta	t-test value	p-value significance
Lipoprotein-associated Phospholipase A2	-0.146	0.022	-0.147	-6.796	0.001
Body Mass Index (kg/m2)	-0.020	.005	-0.202	-4.388	0.001
Systolic Blood Pressure mm Hg	-0.013	.002	-0.271	-5.428	0.001
Metabolic Syndrome	0.137	.044	0.176	3.099	0.002
Creatine kinase myocardial band(ug/L)	-0.126	0.056	-0.118	-2.352	0.019
Calcium (mmol/L)	0.082	.036	0.116	2.277	0.023
Triglyceride (mmol/L)	0.220	.010	-0.111	-2.194	0.029
Total cholesterol (mmol/L)	-0.050	0.020	-0.091	-2.001	0.046