Original Research Article

Lipoprotein-associated Phospholipase A_2 Activity Contributes to the Coronary Artery Disease with Metabolic Syndrome

Running title: LP A_2 activity is a risk for the coronary artery disease with metabolic Syndrome

ABSTRACT

Objective: The aim is to determine contribution of Lp-PLA2 to coronary artery disease (CAD) in patients with and without Metabolic Syndrome (MetSynd)..

Subjects and methods: This is a cohort prospective study based on 412 patients male and female 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.

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, diabetic and stroke. Also, there was a significant difference between MetSynd Positive versus 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-PLA2 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 (/mm3)(p=0.008); Platelet (103/mm3)(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/m2) (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-PLA2 (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-PLA2 nmol/min/Ml (p<0.001), BMI (kg/m2) (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.

Key words: Lipoprotein-associated Phospholipase, A_2 Activity, Coronary Artery Disease, Metabolic Syndrome

Introduction

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].

Inflammation has been increasingly recognised as a critical step in the pathogenesis of both coronary artery disease (CAD) and MetSynd [5-9]. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a novel inflammatory marker associated with MetS, low density lipoprotein (LDL) cholesterol, atherosclerotic disease and incident cardiovascular disease (CVD). Lp-PLA2 has role of proatherogenic, and determine risk factor for CVDr events [10-13]. To the best of our knowledge, it is unclear whether Lp-PLA2 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 the possible contribution of Lp-PLA2 to coronary artery disease in patients with and without MetSynd.

Subjects and Methods

The current study based on cohort design a total of 412 patients and aged from 25 to75 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.3193 and IRB# 10840098-604.01.01-E.8421). Informed consent was obtained from the all patients.

Lp-PLA2 activity assay

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 enzymetic 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 [16-17] and impaired impaired FPG ≥110 mg/dL, impaired PG tolerance (2h PG ≥140 mg/dL) elevated insulin levels (4th quartile of reference). Plus two or more of the following: Systolic BP ≥140 mm Hg and/or, diastolic BP ≥90 mm Hg; [18]; TG ≥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/m2 diagnosed hypertension Microalbuminuria: Urinary albumin excretion rate ≥20 mg/ml or albumin/creatinine ratio ≥30 mg/g

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.

Results

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 .

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 (µIU/dl) (p=0.001); C-reactive protein (mg/L) (p=0.004);White blood cell (/mm3)(p=0.008); Platelet (103/mm3)(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/m2) (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/m2) (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.

Discussion:

This study identified increased total plasma Lp-PLA2 activity in patients with the metabplic Syndrome, especially in those with coronary artery disease when compered 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.

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/m2), 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 (/mm3), vitamin D (ng/ml), hemoglobin A1c (%), vitamin B12, and calcium (mmol/L). Those results are consistents with te Tsimikas et al. Results. [3]. Additionally, this study confirms the strong association between Lp-PLA2 levels and the metabolic syndrome [2, 7].

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 is associated phosholipase 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 agrement between Persson et al [7] Sweden study and current study.

In most recent conducted study [25] that use of postmenopausal hormones, not smoking, and having a BMI less than 25 kg/m^2 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.

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

REFERANCES:

1. Anderson JL. Lipoprotein-associated phospholipase A2: an independent predictor of coronary artery disease events in primary and secondary prevention. Am J Cardiol. 2008 Jun 16;101(12A):23F-33F. doi: 10.1016/j.amjcard.2008.04.015.
2. Svarovskaya AV, Teplyakov AT, Gusakova AM, Garganeeva AA. Role of markers of inflammation and endothelial dysfunction in the prognosis of the development of cardiovascular complications in

patients with coronary artery disease and metabolic syndrome after coronary stenting. Kardiologiia. 2020 Sep 17;60(8):98-105.

3. Tsimikas S, Willeit J, Knoflach M, Mayr M, Egger G, Notdurfter M, Witztum JL, Wiedermann CJ, Xu Q, Kiechl S. Lipoprotein-associated phospholipase A2 activity, ferritin levels, metabolic syndrome, and 10-year cardiovascular and non-cardiovascular mortality: results from the Bruneck study. Eur Heart J. 2009 Jan;30(1):107-15.

4. Bener A, Al-Hamaq AOAA, Zughaier SM, Öztürk M, Ömer A. Assessment of the Role of Serum 25-Hydroxy Vitamin D Level on Coronary Heart Disease Risk With Stratification Among Patients With Type 2 Diabetes Mellitus. Angiology. 2021 Jan;72(1):86-92.

5: Koenig W, Khuseyinova N, Löwel H, Trischler G, Meisinger C. Lipoprotein-associated phospholipase A2 adds to risk prediction of incident coronary events by C-reactive protein in apparently healthy middle-aged men from the general population: results from the 14-year follow-up of a large cohort from southern Germany (MONICA-Augsburg). Circulation 2004;110:1903–1908.

6: Paoletti R, Bolego C, Poli A, Cignarella A. Metabolic syndrome, inflammation and atherosclerosis. Vasc Health Risk Manag. 2006;2(2):145-52. doi: 10.2147/vhrm.2006.2.2.145.

7. Persson M, Hedblad B, Nelson JJ, Berglund G: Elevated Lp-PLA2 Levels Add Prognostic Information to the Metabolic Syndrome on Incidence of Cardiovascular Events Among Middle-Aged Nondiabetic Subjects. Arterioscler Thromb Vasc Biol 2007, 27:1411-1416.

8. Ballantyne CM, Hoogeveen RC, Bang H, Coresh J, Folsom AR, Heiss G, Sharrett AR: Lipoprotein-associated phospholipase A2, high-sensitivity C-reactive protein, and risk for incident coronary heart disease in middle-aged men and women in the Atherosclerosis Risk in Communities (ARIC) Study. Circulation 2004, 109:837-842.

9. Carlquist JF, Muhlestein JB, Anderson JL. Lipoprotein-associated phospholipase A2: a new biomarker for cardiovascular risk assessment and potential therapeutic target. Expert Rev Mol Diagn 2007;7:511-517.

10. Khuseyinova N, Imhof A, Rothenbacher D, Trischler G, Kuelb S, Scharnagl H, Maerz W, Brenner H, Koenig W. Association between Lp-PLA2 and coronary artery disease: focus on its relationship with lipoproteins and markers of inflammation and hemostasis (HELICOR). Atherosclerosis 2005;182:181–188.

11. Daniels LB, Barrett-Connor E, Sarno M, Laughlin GA, Bettencourt R, Wolfert RL. Lipoprotein-associated phospholipase A2 (Lp-PLA2) independently predicts incident coronary heart disease

(CHD) in an apparently healthy older population: the Rancho Bernardo Study. Circulation 2006;114:II-870.

12. Li J, Wang H, Tian J, Chen B, Du F. Change in lipoprotein-associated phospholipase A2 and its association with cardiovascular outcomes in patients with acute coronary syndrome. Medicine (Baltimore). 2018 ;97(28):e11517.
13. May HT, Horne BD, Anderson JL, Wolfert RL, Muhlestein JB, Renlund DG, Clarke JL, Kolek MJ, Bair TL, Pearson RR, Sudhir K, Carlquist JF. Lipoprotein-associated phospholipase A2 independently predicts the angiographic diagnosis of coronary artery disease and coronary death. Am Heart J 2006;152:997–1003.
14. Jenny NS, Solomon C, Cushman M, Nelson JJ, Tracy RP, Psaty BM, Furberg CD. Lipoprotein-associated phospholipase A2 and cardiovascular disease: results from the Cardiovascular Health Study [abstract]. Circulation 2006;113:E-332.
15. Li J, Zhou Z, Niu X, Li H. Lipoprotein-Associated Phospholipase A2 in Cardiac Disease: a Potential Early Biomarker of Unstable Coronary Artery Disease. Clin Lab. 2020 May 1;66(5). doi: 10.7754/Clin.Lab.2019.190719.
16. Alberti KGMM, Zimmet P, Shaw J.Metabolic syndrome - A new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med*. 2006;23 (5):469–480
17. Deedwania PC, Maki KC, Dicklin MR, Stone NJ, Ballantyne CM, Davidson MH. Application of recent definitions of the metabolic syndrome to survey data from the National Cholesterol Education Program Evaluation Project Utilizing Novel E-Technology (NEPTUNE II). J Cardiometab Syndr 2006;1:295–300.
18. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486 –2497.
19-Leipsic J, Abbara S, Achenbach S, Cury R, Earls JP, Mancini GJ,et al. SCCT guidelines for the interpretation and reporting of coronary CT angiography: a report of the Society of Cardiovascular Computed Tomography Guidelines Committee. J Cardiovasc Comput Tomogr 2014;8:342-58
20. Stocker TJ, Bull R, Buls N, Leipsic J, Chow B, Maurovich-Horvat P, Bittencourt MS, Bax JJ, Andreini D, Chen MY, Rubinshtein R, Hadamitzky M, Massberg S, Hausleiter J. Contrast agent

volume for coronary computed tomography angiography imaging in current clinical practice. J Cardiovasc Comput Tomogr. 2021 30:S1934-5925(21)00454-8.

21. Corsetti JP, Rainwater DL, Moss AJ, Zareba W, Sparks CE. High lipoprotein-associated phospholipase A2 is a risk factor for recurrent coronary events in postinfarction patients. Clin Chem 2006;52:1331-1338.
22. Sabatine MS, Morrow DA, O'Donoghue M, Jablonski KA, Rice MM, Solomon S, Rosenberg Y, Domanski MJ, Hsia J, for the PEACE Investigators. Prognostic utility of lipoprotein-associated phospholipase A2 for cardiovascular outcomes in patients with stable coronary artery disease. Arterioscler Thromb Vasc Biol 2007; 27:2463–2469.
23. Sairam SG, Sola S, Barooah A, Javvaji SK, Jaipuria J, Venkateshan V, Chelli J, Sanjeevi CB. The role of Lp-PLA_2 and biochemistry parameters as potential biomarkers of coronary artery disease in Asian South-Indians: a case-control study. Cardiovasc Diagn Ther. 2017 Dec;7(6):589-597..
24. Mockel M, Muller R, Vollert JO, Muller C, Danne O, Gareis R, Stork T, Dietz R, Koenig W. Lipoprotein-associated phospholipase A2 for early risk stratification in patients with suspected acute coronary syndrome: a multi-marker approach: the North Wuerttemberg and Berlin Infarction Study-II (NOBIS-II). Clin Res Cardiol 2007;96:604 – 612.
25. Hatoum IJ, Nelson JJ, Cook NR, Hu FB, Rimm EB. Dietary, lifestyle, and clinical predictors of lipoprotein-associated phospholipase A2 activity in individuals without coronary artery disease. Am J Clin Nutr. 2010 Mar;91(3):786-93.

Table 1. Socio-demographic characteristics of patients by metabolic syndrome (N = 412)

Variables		Metabolic Syndrome Positive n = 126 (%)	Metabolic Syndrome Negative n = 286 (%)	*p*-value Significanc
Age group				
	<40	34 (27.0)	82 (28.7)	
	40-49	34 (27.0)	45 (15.7)	**0.025**
	=>50	58 (46.0)	159 (55.6)	
Gender				
	Male	89 (70. 6)	150 (52.4)	**0.001**
	Female	37 (29.4)	136 (47.6)	
BMI (25 kg/m$^{2)}$				
	Normal (<25 kg/m^2)	25 (19.8)	91 (40.9)	
	Overweight (29-30 kg/m	57 (45.2)	117 (27.3)	**0.037**
	Obese (>30 kg/m^2)	44 (34.9)	78 (30.1)	
Cigarette Smoke				
	Yes	35 (27.8)	49 (17.1)	**0.013**
	No	91 (72.2)	237 (82.9)	
Nargile-smoking	Yes	21 (16.7)	24(8.4)	**0.012**
	No	105 (83.3)	262 (91.6)	
Diabetes				
	Yes	27 (21.4)	30 (10.5)	**0.003**
	No	99 (78.6)	256 (89.5)	
Thyroid				
	Yes	38 (30.2)	113 (24.6)	**0.002**
	No	88 (69.8)	346 (75.4)	
Chronic Obstructive Pulmonary Disease				
	Yes	30 (23.8)	37 (12.9)	**0.005**
	No	96 (76.2)	249 (87.1)	
Hypertension				
	Yes	43 (34.1)	64 (22.4)	**0.009**
	No	83 (65.9)	222 (73.6)	
Coronary Artery Disease				
	Yes	65 (51.6)	103 (36.0)	**0.003**
	No	61 (48.4)	183 (84.0)	
Stroke				
	Yes	32 (25.4)	91 (31.8)	0.201
	No	94 (74.6)	195 (68.2)	
Coronary Heart Failure				
	Yes	43 (34.1)	69 (24.1)	
	No	83 (65.9)	217 (75.9)	**0.025**

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

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

+

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

Variables	Metabolic Syndrome Positive = 126 Mean ± SD	Metabolic Syndrome Negative = 286 Mean ± SD	p value
Creatine kinase (ug/L)	40.47± 23.71	38.54± 20.55	0.403
Creatine kinase-myocardial band; (ug/L)	15.21± 8.96	12.74± 5.66	**0.001**
Lp-PLA2 activity (mmol/min/L)	647.92±153.50	593.90±146.27	**0.001**
HOMA-IR index	2.80± 1.63	2.30± 1.59	**0.004**
Insulin (µIU/dl)	11.31±3.88	10.41±4.27	**0.001**
C-reactive protein (mg/L)	13.56±5.01	11.92±7.42	**0.004**
White blood cell (/mm3)	7455.63±1715.00	7906.3±1495.25	**0.008**
Neutrophil (/mm3)	5.435±3.02	5.44±3.17	0.952
Lymphocyte (/mm3)	1.93±0.93	1.98±0.96	0.587
Platelet (103/mm3)	243.31±97.03	267.72±95.57	**0.018**
Mean Plate Volume (mg/L)	9.77±1.15	9.99±0.82	**0.032**
Mean corpuscular volume (mg/L)	85.98±7.84	88.8±5.20	0.542
Red cell distribution width (mg/L)	13.48±1.50	14.26±2.06	**0.001**
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)	**0.019**
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 İndex (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 İndex (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