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Original Article

Evaluation of OxPL Levels in Patients Undergoing Coronary Angiography: A Cross-Sectional Study

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Abstract

Background and Aim: Coronary ectasia is one of the prevalent cardiovascular diseases worldwide. It causes many deaths annually ranged between 9% to 10% which is dependent on related risk factors. The main pathogenesis has not been determined yet; however, it has been shown, that increased lipid profiles and their oxidation in patients can cause endothelial cell dysfunction and thrombosis. Therefore, here we investigated the oxidized phospholipids (OxPLs) role in the pathogenesis of coronary artery disease.

Methods: This cross-sectional study was performed in Shariati Hospital, Tehran. Accordingly, patients with coronary artery angiography indications (n=360) were included and classified into one of the following three groups, based on the angiographic results: 1) normal coronary artery (not dysfunction in vessels) or mild CAD (only intimal irregularity or less than 3% narrowing without ectasia); 2) vessel dilation more than 1.5 times compared to the normal part of the vessel or compared to the normal size according to age and gender in one or more coronary vessels; and 3) patients with more than 50% stenosis in one of the coronary arteries. The peripheral blood was collected from patients in EDTA anticoagulants container tubes and the OxPL level was measured using an ELISA kit.

Results: The results showed that the amount of OxPL in the third and second groups was higher than in the first group. It was also found that hyperlipidemia, diabetes, hypertension, and smoking were higher in the third and second groups; all mentioned findings were statistically significant (p-value <0.05).

Conclusion: According to the findings of this study, it was shown that an increase in OxPL in patients with coronary ectasia can be considered as a risk factor for disease progression; OxPL measurement can be used to identify high-risk individuals.

Keywords: Coronary Ectasia; Risk Factor; Oxidative Phospholipid; Angiography.

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Introduction

Coronary ectasia is a cardiovascular disease (CVD) characterized by endothelial cell (EC) dysfunction (1). Due to the increasing prevalence of CVD and related mortality, identification of the risk factors and effective elements in their pathogenesis is an important matter (2, 3). Today, many factors have been identified to the pathogenesis of coronary ectasia; however, the main factor involved in the occurrence and progression of the disease has not been identified (4, 5).

Inflammation is one of the factors influencing CVD development, especially coronary ectasia (6, 7). According to the inflammation role, it has been found that immune system cells and platelets, due to inflammatory mediators secretion and stimulating the immune response, lead to immune

system cells movement towards ECs; it impairs ECs function (8, 9).

Oxidized phospholipids (OxPLs) play an important role in the pathogenesis of coronary ectasia as pro-inflammatory factors (10). Therefore, it has been shown that increased lipid factors and inflammation in patients with coronary ectasia lead to increased OxPLs serum levels (11-13). Hence, we decided to evaluate the relationship between OxPLs levels and patients' clinical symptoms in the present study.

Methods

This cross-sectional study was approved by the Ethics Committee of the Vice Chancellor for Research of Tehran University of Medical Science (IR.TUMS.THC.REC.1399.058). It was performed on patients with Coronary Ectasia referred to Shariati Hospital in Tehran, Iran during 2018-2020.

The study population included patients, who were candidates for coronary angiography. Inclusion criteria were as follows: patients with complete case information and without any underlying diseases, using drugs such as calcium channel blockers, angiotensin-converting enzyme inhibitors, aspirin, and anti-lipids. Exclusion criteria were patients with incomplete case information and the presence of underlying disease. In this study, patients were classified into one of the following three groups, based on the angiographic results: 1) normal coronary artery (not dysfunction in vessels) and mild CAD (only intimal irregularity or less than 3% narrowing without ectasia); 2) vessel dilation more than 1.5 times compared to the normal part of the vessel or compared to the normal size according to age and gender in one or more coronary vessels; 3) patients with stenosis of more than 50% in one of the coronary arteries.

Background information such as age, gender, body mass index, information about clinical records, and cardiovascular risk factors were all collected through interviews or reviewing patients' archives. Before angiography, blood samples were taken and OxPL levels in apoB-100 lipoprotein were evaluated using E06 monoclonal antibody and ELISA (Roche, Germany). In the next step, patients were classified based on the coronary angiography results into one of the mentioned groups.

Statistical Analysis

For quantitative variables, mean or median, and standard deviation or interquartile range were used to describe variable distributions. Frequency and percentage were used for qualitative variables. Normal distribution was checked using the Kolmogorov-Smirnov test. Independent t-test and Mann-Whitney U test were used for univariate data analysis. The significance level was considered 0.05. All analyzes were performed using SPSS software version 22.

Results

In this study, after assessing 360 patients, 120 patients were evaluated in each group. Clinical and demographic information of patients has been listed in Table 1.

As shown in table 1, there were no significant differences between patients' ages in all three groups. Also, there were no significant differences in terms of BMI and systolic and diastolic blood pressure between the patients in the three groups. The percent of diseases such as diabetes, hyperlipidemia, and also smoking was statistically higher in the third group compared to the other two groups (p-value <0.05).

Evaluation of OxPL and Lipid profiles in three groups

The results showed that the amount of HDL in the first group was higher, but this difference was not statistically significant (p-value: 0.24). On the other hand, it was found that LDL, Total cholesterol, and OxPL levels were higher in the third group, which was statistically significant (p-values <0.05) (Table 2).

Association between OxPL level and disease severity

Based on the results, OxPL levels were higher in the third and second groups compared to the first group of patients with a history of diabetes mellitus, which was statistically significant (p-value: 0.02). On the other hand, it was found that the OxPL level was higher in the third group of patients with a history of smoking and hyperlipidemia compared to the other two groups (p-value <0.05). The OxPL

level was the same in the second and the third groups of patients with the hypertension history, and it was higher than the first group; it was also statistically significant (p-value <0.05) (Table 3).

Table 1. Demographic and clinical information of patients (n=360).

Variables		Group I (n=120)	Group II (n=120)	Group III (n=120)	P-value*
Age (year)		60.0 ± 10.9	59.6 ± 11.1	60.6 ± 10.7	0.1
Gender (Male/Female %)		24.2/75.8	62/38	76.4/23.6	0.01
BMI (Kg/m^2)		27.1±3.6	27.1±4.2	29.5±4.8	0.3
Hypertension		66	74	94.2	0.02
Diabetes Mellitus (%)	**Yes**	42.4	46	59.4	0.04
	No	57.6	54	40.6	
Smoking (%)	**Yes**	15.2	37	43.4	0.01
	No	84.8	63	56.6	
Hyperlipidemia (%)	**Yes**	54.4	60	89	0.03
	No	45.6	40	11	
Systolic blood pressure (mmHg)		147.4 ±20.3	149.3 ±20.4	152.3 ±22.4	0.3
Diastolic blood pressure (mmHg)		86.9 ±9.3	87.0 ±9.3	87.1 ±9.5	0.1

*P-value calculated by T-test or Chi-Square.

Table 2. Levels of OxPL and Lipid profiles in the studied groups (n=360).

Variables	Group III (n=120)	Group II (n=120)	Group I (n=120)	P-value*
HDL (mg/dL)	59.2±16.2	54.9±15.2	56.9±18.2	0.24
LDL (mg/dL)	143.8±37.5	155.8±39.5	161.3±36.5	0.007
Total Cholesterol (mg/dL)	228.4±42.0	240.7±43.8	245.6±42.1	0.013
OxPL	0.3	0.5	0.9	0.01

Abbreviations: HDL: High-density lipoprotein; LDL: low-density lipoprotein, OxPL: Oxidized Phospholipids.
*P-value calculated by ANOVA.

Table 3. Level OxPL in three groups according to smoking and conditions of diseases

Variables		Group I (n=120)	Group II (n=120)	Group III (n=120)	P-value*
Diabetes Mellitus (%)	**Yes**	0.3	0.4	0.08	0.02
	No	0.2	0.2	0.4	
Smoking (%)	**Yes**	0.2	0.4	0.7	0.04
	No	0.04	0.2	0.3	
Hyperlipidemia (%)	**Yes**	0.4	0.6	0.9	0.01
	No	0.1	0.3	0.4	
Hypertension (%)	**Yes**	0.2	0.3	0.°	0.01
	No	0.01	0.1	0.09	

*P-value calculated by ANOVA.

Discussion

Coronary artery disease and coronary ectasia are the most common vascular diseases in which the main arteries that carry blood, oxygen, and nutrients to the heart become clogged due to the deposition of plaques containing fat, cholesterol, calcium, and

other substances in the blood. Lack of blood supply and adequate oxygen for the heart leads to myocardial infarction and even death (9, 14).

Coronary artery diseases have well-known risk factors, such as hyperlipidemia, hypertension, diabetes mellitus, obesity, poor diet, and smoking (2, 15). In addition to the changing dietary patterns of individuals in the last decade, new risk factors such as oxidative stress and their relationship with the incidence of cardiovascular disease have been studied. With the aim of treatment and prevention, studies have examined several mechanisms for rooting out the disease; oxidative stress is one of the most important mechanisms (6, 16).

Recent studies have shown, that lipid profiles and oxidative stress are closely related. Based on this, it has been found that oxidative stress increment can increase the oxidation of fats and phospholipids; it leads to the production of oxidized products such as OxPL and ox-LDL (16-18). However, few studies have been performed on the role of these agents, especially OxPL in the pathogenesis of coronary ectasia. Therefore, in this study, we aimed to evaluate the relationship of OxPL with the pathogenesis of coronary artery ectasia.

The results of the present study showed, that OxPL in patients with stenosis of more than 50% in one of the coronary arteries, and patients with coronary vessel dilation, was significantly higher than patients with normal vessels or mild CAD.

In 2017, Kamstrup et al. conducted a study to evaluate the association of OxPL with cardiovascular disease in patients with coronary heart disease and healthy individuals. The results showed a significant correlation between apolipoprotein (a) and OxPL-apoB markers. OxPL-apoB levels were significantly associated with coronary heart disease risk factors. A simultaneous increase in the serum levels of OxPL-apoB and apolipoprotein (a) also doubles the risk of coronary heart disease (19).

In another study by Tsimikas et al., serum levels of OxPL bound to apolipoprotein B-100 or OxPL / apoB, as well as Lp (a), were assessed in patients undergoing coronary angiography. Moreover, IL-1 genotypes were also examined. Among patients with IL-1 (+), the highest OxPL/apoB quartile was associated with an increased risk of coronary heart disease-related to its lowest quartile. This effect was relatively more severe in patients under the age of 60. In patients with IL-1 (-), OxPL/apoB had no significant correlation with the coronary heart disease risk. In IL-1 (+) patients, the median OxPL/apoB was also a predictor of four-year cardiac-free survival in patients with coronary heart disease (20, 21).

In another study, which evaluated patients with sudden cardiac death due to coronary artery occlusion and successfully treated patients with PCI, serum OxPL / apoB level was assessed before and up to one week after the PCI treatment. First, the coronary artery IHC technique showed high levels of OxPL and MDA-shaped epitopes, especially in the recanalized region and organized thrombosis. Following PCI, serum levels of OxPL / apoB and Lp (a) gradually increased and reached the maximum level after 7 days. In contrast, OxPL / apoB and Lp (a) increased immediately after PCI in the non-involved vessels but returned to the baseline rapidly within 24 hours (22).

The previous history of several diseases is another risk factor for disease progression in patients with coronary heart disease and ectasia. A study by Tsimikas et al. showed that people with a history of hyperlipidemia, as well as higher lipid profiles, including LDL and triglycerides, had increased OxPL levels.

Finally, it was concluded that lipid profiles increment, as a risk factor, increases the OxPL in patients; it ultimately leads to disease progression and endothelial cell dysfunction (22). In the study of Kiechl et al., it was found that previous history of diabetes, hypertension, smoking, and hyperlipidemia in patients can increase the coronary artery disease progression in patients with coronary ectasia (23).

Conclusion

According to the findings of this study, it was shown that an increase in OxPL in patients with coronary ectasia can be considered as a risk factor for disease progression; OxPL measurement can be used to identify high-risk individuals.

Conflict of Interest

The authors declared that they have no conflict of interest.

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Ethics

This cross-sectional study was approved by the Ethics Committee of the Vice Chancellor for Research of Tehran University of Medical Science (IR.TUMS.THC.REC.1399.058).

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