Paraoxonase Activity and Oxidized LDL Levels as Cardiovascular Risk Factors in Patients with Coronary Artery Disease

Koroner Arter Hastalarında Kardiyovasküler Risk Faktörü Olarak Paraoksonaz Aktivitesi ve Okside LDL Düzeyleri

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Objective: The aim of this study was to investigate the possible relationship between serum oxidized low-density lipoprotein (Ox-LDL) concentration, recently shown to be a cardiovascular risk factor, paraoxonase 1 (PON1) activity and Thiobarbituric Acid Reactive Substance (TBARS) levels, and the severity of Coronary Artery Disease (CAD) as determined by the obstructive vessel number inpatients.

Methods: We determined plasma PON1 activity, serum Ox-LDL concentration, Apolipoprotein A1 (ApoA1) levels, TBARS levels and lipid profiles, including total cholesterol (TC), triglycerides (TG), Low-Density Lipoprotein cholesterol (LDL-C), High-Density Lipoprotein cholesterol (HDL-C), and Very Low-Density Lipoprotein cholesterol (VLDL-C), in patients with CAD (n=42) and in a healthy control group (n=17). The CAD group was divided into three subgroups with single- (n=13), double- (n=15) and triple-vessel (n=14) disease according to their angiography results. PON1 activity and TBARS levels were measured spectrophotometrically; Ox-LDL levels were determined by ELISA; ApoA1levels were determined immunoturbidometrically; and TC, TG, and HDL-C levels were determined enzymatically.

Results: In the study we observed that PON1 activity decreases when the number of affected vessels increases (r=-0,537, p<0.01). Ox-LDL levels in single-, double- and triple-vessel disease groups and in the total CAD group were significantly higher than in the healthy control group (p <0.01). TBARS levels in single-, double- and triple-vessel disease groups were significantly higher than the healthy control group (p<0.01). Moreover, ApoA1 levels in the single-, double- and triple-vessel disease groups were significantly lower than in the healthy control group (p<0.01).

Conclusion: Our results show that low PON1 activity, high Ox-LDL levels, high TBARS levels and low ApoA1 levels may play an important role in the pathogenesis of CAD.

Key Words: PON1, protein, human, oxidized low-density lipoprotein, Thiobarbituric Acid Reactive Substances

Amaç: Bu çalışmada koroner arter hastalarında damar tıkanıklığının şiddetine bağlı olarak serum Okside LDL (Ox-LDL) konsantrasyonu; son zamanlarda kardiyovasküler risk faktör olarak tanımlanan Paraoksonaz 1 (PON1) aktivitesi ve tiobarbitürik asit reaktif substansları (TBARS) düzeyleri arasındaki olası ilişki araştırıldı.

Yöntemler: Okside LDL, Apolipoprotein AI (Apo AI), TBARS düzeyleri, PON1 aktivitesi lipid profili (Total Kolesterol (TK), Trigliserid (TG), LDL Kolesterol (LDL-K), HDL Kolesterol (HDL-K), VLDL Kolesterol (VLDL-K) düzeyleri 42 koroner arter hastası ve 17 sağlıklı bireyde belirlendi. Hasta grubu anjiografi sonuçlarına göre tek damar (n:13), iki damar (n:15) ve üç damar (n:14) olarak 3 alt gruba bölündü. PONI aktivitesi ve TBARS düzeyleri spektrofotometrik, Ox-LDL düzeyleri Eliza, Apo-AI immunoturbidimetrik, TK, TG ve HDL-K düzeyleri ise enzimatik yöntemlerle tayin edildi.

Bulgular: Çalışmamızda damar tıkanıklık derecesi arttıkça PON1 aktivitesinin azaldığı gözlendi (r: -0,537, p<0,01). Tek damar, iki damar, üç damar ve total hasta grubunda Ox-LDL düzeyleri kontrol grubuna göre istatistiksel olarak yüksek bulundu (p<0,01). TBARS düzeyleri tek, iki ve üç damar tıkanıklığı bulunan hasta grubunda kontrol grubuna göre istatistiksel olarak anlamlı düzeyde yüksek bulundu (p<0,01). Tek, iki ve üç damar tıkanıklığı bulunan bireylerde Apo AI düzeyleri ise kontrol grubundan düşük bulundu (p<0,01).

Sonuç: Sonuçlarımız düşük PON1aktivitesi, yüksek Ox-LDLve TBARS düzeyleri, düşük Apo AI düzeylerinin koroner arter hastalığının patogenezinde önemli rol oynayabileceğini göstermektedir.

Anahtar Kelimeler: PON1, protein, insan, okside LDL, tiobarbitürik asit reaktif substansları

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Introduction

CAD is the major cause of death in North America and the rest of the western world. It is also being recognized as an important contributor to morbidity and mortality in the developing countries of the world. CAD is a multifactorial disease. Elevated levels of TC and LDL-C and low levels of HDL-C have been reported as the most important risk factors for CAD. Enhanced formation of reactive oxygen species (ROS) may affect four fundamental mechanisms that contribute to atherogenesis, namely: oxidation of low-density lipoprotein (LDL), endothelial dysfunction, vascular smooth muscle cell growth, and monocyte migration (1, 2).

The formation of Ox-LDL is an indiscernible reaction that causes altered membrane proteins and phospholipids, and increased expression of signaling molecules that recruit monocytes (3). Membrane damage caused by Ox-LDL impairs endothelial function. Attempts to measure plasma levels of Ox-LDL have been reported (4, 5).

PON1 (EC 3.1.8.1) is an HDL-associated arylesterase that hydrolyzes paraoxon, the active toxic metabolite of the organophosphate parathion. Serum PON1 is associated with high-density lipoprotein (HDL). PON1 functions in preventing lipid oxidation not only of LDL, but also of HDL itself (6). This protection is most probably related to the PON1-hydrolyzing activity of some activated phospholipids and/or lipid peroxide products (7, 8). The free thiol at cysteine-284 of PON1 is required to prevent

LDL oxidation and is thought to be the active site for the antioxidant activity of PON1 (9). There is now growing evidence that PON1 plays an important role in lipoprotein metabolism and thus may affect the risk of CAD and atherosclerosis in the general population (10).

To our knowledge, no previous studies have investigated the changes in PON1 activity and the circulating Ox-LDL and TBARS levels in patients with angiographically defined CAD. The aim of this study was to investigate the possible relationship between serum Ox-LDL concentration, recently shown to be a cardiovascular risk factor, and PON1 activity and TBARS levels in patients with angiographically defined CAD.

Methods

Subjects
The profiles of the study population are presented in Table 1. The study groups included patients with CAD (n=42) and the healthy control group (n=17). The patient group was divided into three subgroups with single- (n=13), double- (n=15) and triple-vessel (n=14) disease according to their angiography results. Diagnostic coronary arteriography was carried out using the Judkins technique and all the coronary angiograms were determined visually by two different cardiologists. The severity of coronary artery stenosis was assessed and classified according to the American Heart Association System (AHA) (11). According to AHA, significant angiographic coronary stenosis is defined as the presence of stenosis in excess of 70% of the luminal diameter. Multi-vessel disease was defined as the presence of significant stenoses in more than 1 of the 3 major epicardial coronary arteries. All subjects were examined by a cardiologist and information on medical histories, habits and medications was obtained via a questionnaire. The following conventional cardiovascular risk factors were defined (12): arterial hypertension (systolic blood pressure > 140 mm Hg and/or diastolic blood pressure > 90mm Hg and/or use of antihypertensive drugs), dyslipidemia (TC ≥ 200 mg/dL and/or LDL-C ≥ 130 mg/dL and/or use of cholesterol lowering drugs), diabetes (fasting glucose ≥ 127 mg/dL and/or use of pharmacological treatment), family history of cardiovascular disease (symptomatic CAD occurring in first-degree male relatives aged < 55 years or first-degree female relatives aged < 65 years), obesity (body mass index, BMI ≥ 30 kg/m^2) and smoking (regular smoking or quitting < 3 months ago). Exclusion criteria were the presence of neoplastic diseases, concomitant inflammatory diseases such as infections and auto-immune disorders, major depression, liver and kidney diseases and recent major surgical procedures. The healthy control group was enrolled from non-medical staff of the hospital and their relatives, and was selected to match the CAD group by gender and age. For inclusion into the control group, subjects were selected who had no known coronary risk factors or cardiac symptoms, normal electro-cardiographic and echo-cardiographic examinations and negative exercise stress tests. Coronary angiography was not performed on the control group. All the subjects gave informed consent prior to the study.

Peripheral venous blood samples were drawn from all subjects after an overnight fast to analyze all parameters. Plasma samples for PON1 activity determination were collected from 0.5 ml 3.8% citrate / 5 mL of venous blood. following centrifugation at 3500 g for 15 minutes (min). Serum samples for the determinations of Ox-LDL and lipids were obtained from venous blood after a 12 hour (h) fasting period by centrifugation of the clotted specimen within 30 min of collection. The separated plasma and serum was stored in several small aliquots at -80 ºC until assayed. All icteric or haemolytic blood samples were discarded. All reagents were analytical grade and were purchased from Sigma Chemical Company (St. Louis, MO, USA) and Merck (Darmstadt, Germany). All the healthy control and CAD patient samples were collected as outlined in the protocol above and the parameters measured and analyzed simultaneously.

Assay of TBARS:
Lipid peroxidation levels were measured with the Thiobarbituric Acid (TBA) reaction by the method of Angel (13). This method was used to obtain a spectrophotometric measurement of the color produced during the reaction to TBA with TBARS at 535 nm. TBARS concentration was calculated using 1.56×10^{-5} $M^{-1}cm^{-1}$ as the mol/L extinction coefficient. The results were expressed as micromolar (µM).

Assay of PON1 activity:
PON1 activity was assayed using synthetic paraoxon (diethyl-p-nitrophenyl phosphate) as the substrate. PONl activity was determined by measuring the initial rate of substrate hydrolysis to p-nitrophenol with absorbance monitored at 412 nm using an assay mixture containing 2 mM paraoxon, 2 mM CaCl$_2$ and 20 mL of plasma in 100 mM Tris-HCl buffer (pH 8.0). The blank sample containing incubation mixture without plasma was run simultaneously to correct for spontaneous substrate breakdown. The enzyme activity was calculated from E412 of p-nitrophenol (18.290 per M/cm) and was expressed as U/mL; 1 U of enzyme hydrolyses 1 nmol of paraoxon/min (14, 15).

Assay of Ox-LDL:
The concentration of Ox-LDL in serum was measured by a sandwich ELISA kit (Mercodia, Uppsala, Sweden). Briefly, the procedure was conducted using the murine monoclonal antibody, mAb-4E6 as the capture antibody bound to microtitration wells and a peroxidase-conjugated anti-apolipoprotein B antibody recognizing Ox-LDL bound to the solid phase.

Assay of ApoA1 and Lipid Parameters:
ApoA1 measurement was performed by the immunoturbidimetric assay kit (Diasis, İstanbul, Turkey).

Table 1. Profile of the study population

	Healthy individuals	CAD patients
Number	17	42
Age (Years)		
Mean±SD	53.88±8.97	54.59±6.87$^{£}$
Range	39-73	43-72
Gender		
Male, n (%)	9 (52.94)	31(73.81)
Female, n (%)	8 (47.06)	11(26.19)
BMI	24.14±2.06	25.26±2.83$^{£}$
Smoker	-	17
DM	-	5
HT	-	4

BMI: body mass index, DM: diabetes mellitus, HT: hypertension, $^{£}$Not significant

TC, TG and HDL-C were determined by routine laboratory methods using the Hitachi 704 autoanalyzer (Boehringer Mannheim, Tokyo, Japan). HDL-C was measured after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungistic acid. LDL-C was calculated using the Friedewald formula.

Statistical analysis
Conventional methods were used for the calculation of the mean, and the standard errors of the mean (SEM). The data are expressed as the mean±SEM. The significance of differences between variables of the CAD and the healthy control groups was determined by the Student's t-test, Mann-Whitney U test, One-Way Analysis of Variance (ANOVA), and Bonferroni's t-test. For correlation analysis, Pearson and Spearman correlations were used. P values ≤ 0.05 were considered significant.

Results

Results of Ox-LDL, TBARS, PON1, and ApoA1 levels in the CAD patient and healthy control groups are presented in Table 2. The average serum Ox-LDL levels in the CAD patient group were significantly higher than in the healthy control group (p<0.01). Moreover, in CAD patients with single-, double- and triple-vessel disease, serum Ox-LDL levels were found to be significantly higher than in the healthy control group (p<0.01). Furthermore, serum TBARS levels in patients with CAD were found to be significantly higher than those in the healthy control group (p<0.01). However, we could not find any significant differences in TBARS levels between the CAD patient subgroups.

In our study, plasma PON1 activities in patients with CAD were found to be significantly lower than those in the healthy control group (p<0.01). In CAD patients with double- (p<0.01) and triple-vessel (p<0.01) disease, plasma PON1 activities were found to be significantly lower than in the healthy control group. In addition, in CAD patients with single-vessel disease, plasma PON1 activities were found to be significantly higher than in the double- (p<0.05) and the triple-vessel (p<0.01) CAD patient groups.

The average serum ApoA1 levels in the CAD patient group of single-, double- and triple-vessel disease subgroups were lower than those in the healthy control group (p<0.01). In addition, the average serum ApoA1 levels in CAD patients with double-vessel disease were found to be significantly higher than in CAD patients with triple-vessel disease (p<0.05).

Table 3 lists serum TG, TC, HDL-C, LDL-C, and VLDL-C levels in patients with CAD and in the healthy control groups. In the CAD patient group, TG levels were found to be significantly higher than those in the heathy control group. However, we could not find any significant differences in TC and LDL-C levels between the CAD patients and the healthy control group. In addition, in patients with CAD, serum HDL-C levels were found to be significantly lower than in the healthy control group (p<0.01). However, there was no significant difference in serum HDL-C levels between CAD patients with single-, double- or triple-vessel disease.

Table 4 shows the LDL-C/HDL-C, TC/HDL-C, and Ox-LDL/LDL-C ratios in patients with CAD and in the healthy control group. LDL-C/HDL-C (p<0.01), TC/HDL-C (p<0.01), and Ox-LDL/LDL-C (p<0.01) ratios were found to be significantly higher in the CAD patients than in the healthy control group.

Table 5 shows the ApoA1/PON1, HDL-C/PON1, and HDL-C/ApoA1 ratios in patients with CAD and in the healthy control group. ApoA1/PON1 (p<0.01) and HDL-C/PON1 (p<0.01) ratios were found to be significantly higher in the CAD patients than in the healthy control group.

Table 2. Comparison of Ox-LDL, TBARS, PON1, and Apo A1 levels in patients with CAD and in the control group

Group	N	Ox-LDL (U/L)	TBARS (µM)	PON-1 (U/mL)	Apo A1 (mg/dL)
Control	17	33.19±7.76	4.66±1.07	131.40±46.75	114.41±9.94
1 Vessel	13	59.60±10.77[a]	7.65±1.49[a]	97.75±19.38[1, Ω]	81.54±13.11[a]
2 Vessel	15	58.74±9.19[a]	8.71±2+25[a]	60.19±33+09[2]	91+47 ±16+92[a,b]
3 Vessel	14	64.72±9.95[a]	8.07±1.71[a]	52+11±23+97[2]	77.64±11+35[a]
All patients	42	61.00±10+07[*]	8+17±187[*]	69+12±32.46[*]	83.79±15.00[*]

[a]p<0.01 (1, 2, 3 Vessel-Control), [1]p<0.05 (1 Vessel-2 Vessel), [*]p<0.01 (All patients-Control), [2]p<0.01 (2, 3 Vessel-Control), [Ω]p<0.01 (1 Vessel-3 Vessel), [b]p<0.05 (2 Vessel-3 Vessel)

Table 3. Comparison of triglyceride, total cholesterol, HDL, LDL and VLDL cholesterol levels in patients with CAD and in the control group

Group	N	TG (mg/dL)	TC (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)
Control	17	78.35±43.30	180.59±25.79	52.65±12.43	112.27±21.84	15.67±8.66
1 Vessel	13	111.77±40.98	187.92±28.64	42.23±9.86[1]	123.34±26.39	22.35±8.20
2 Vessel	15	127.33±53.12[a]	184.60±19.28	43.00±9.24	116.13±19.99	25.47±10.62[a]
3 Vessel	14	103.07±47.97	191.36±37.85	41.50±9.09[2]	129.24±38.48	20.61±6.59
All patients	42	114.43±47.87[b]	187.88±28.80	42.26±9.18[b]	122.73±28.98	22.89±9.57[b]

[a]p<0.05 (2 Vessel-Control), [2]p<0.05 (3 Vessel-Control), [b]p<0.01 (All patients-Control, [1]p=0.051 (1 Vessel-Control)

In Table 6, the Pearson correlation results are shown in patients with CAD. We found a significant negative correlation between HDL-C and Body Mass Index (BMI) (r= -0.331; p<0.05).

Moreover, we have also found significant correlation between some lipid parameters. In addition, there was a negative but statistically insignificant (r=- 0.173; p>0.05) correlation between Ox-LDL and PON1 activity.

On the other hand, according to the Spearman correlation test, there was a strong negative correlation between PON1 and the extent of disease (r=-0.537; p<0.01). In addition, there was a positive but statistically insignificant (r= 0.234; p>0.05) correlation between Ox-LDL levels and the severity of disease.

Discussion

Reactive oxygen species (ROS) production is induced under several pathological conditions by various stimuli. Risk factors for atherosclerosis, such as hypertension and hyperlipidemia, are also associated with increased generation of ROS, and it is likely that cigarette smoking and diabetes mellitus share oxidative heritages (16). A number of studies suggest that ROS oxidize lipids and that Ox-LDL is a more potent pro-atherosclerotic mediator than the native, unmodified LDL (17). The suggestion is based on the observations that high plasma levels of Ox-LDL are present in patients with atherosclerosis and that antibodies to Ox-LDL are detected in the plasma of most patients with atherosclerosis (18).

The average plasma Ox-LDL levels in the CAD patient group were significantly higher than in the healthy control group. Moreover, in patients with single-, double- and triple-vessel disease, plasma Ox-LDL levels were found to be significantly higher than in the healthy control group. These results are in agreement with those reported by Hasegawa et al. (19). This observation strongly suggests that Ox-LDL in circulating serum could serve as a marker for cardiovascular

Table 4. TC/HDL-C, LDL-C/HDL-C, and Ox-LDL/LDL-C ratios in patients with CAD and in the control group

Group	N	TC/HDL-C	LDL-C/HDL-C	Ox-LDL/LDL-C
Control	17	3.57±0.83	2.24±0.67	0.30±0.08
1 Vessel	13	4.56±0.70[a]	3.00±0.67	0.50±0.12[#]
2 Vessel	15	4.50±1.10	2.87±0.99	0.53±0.15[#]
3 Vessel	14	4.77±1.21[b]	3.22±1.06[1]	0.53±0.13[#]
All patients	42	4.60±1.02[2]	3.03±0.92[2]	0.52±0.13[#]

[a]p=0.051 (1 Vessel-Control), [1]p<0.05 (3 Vessel-Control), [b]p<0.01 (3 Vessel-Control), [2]p<0.01 (All patients-Control), [#]p<0.01 (1, 2, 3 Vessel, and All patients-Control)

Table 5. Apo A1/PON1, HDL-C/PON1, and HDL-C/Apo A1 ratios in patients with CAD and in the control group

Group	N	Apo A1/PON 1	HDL-C/PON 1	HDL-C/APO A1
Control	17	0.94±0.22	0.43±0.16	0.46±0.10
1 Vessel	13	0.86±0.201	0.44±0.091	0.52±0.12
2 Vessel	15	1.91±0.97a	0.94±0.532	0.49±0.15
3 Vessel	14	1.78±0.84a	0.94±0.392	0.55±0.18
All patients	42	1.54±0.88a	0.79±0.452	0.52±0.15

[a]p<0.01 (2, 3 Vessel, and All patients-Control), [1]p<0.01 (1 Vessel-2, 3 Vessel), [2]p<0.01 (2, 3 Vessel, and All patients-Control)

Table 6. Pearson correlation results in patients with CAD

	PON1	Ox-LDL	APO A1	TBARS	TC	TG	HDL -C	LDL-C	VLDL-C	BMI
PON1	-	-0.173	0.207	-0.034	-0.196	-0.011	0.048	-0.206	-0.011	0.135
Ox-LDL		-	-0.217	0.148	0.042	-0.122	-0.014	0.086	-0.122	-0.135
APO A1			-	0.236	0.018	0.123	-0.022	-0.016	0.123	0.020
TBARS				-	-0.026	-0.145	-0.068	0.044	-0.145	0.282
TC					-	-0.085	0.295	0.928**	-0.085	0.076
TG						-	-0.317*	-0.314*	1.000**	0.146
HDL-C							-	0.081	-0.317*	-0.331*
LDL-C								-	-0.314	0.132
VLDL-C									-	0.146
BMI										-

[a]p<0.05, **p<0.01

APOA1: Apoprotein A1, BMI: Body Mass Index, HDL-C: HDL cholesterol, LDL-C: LDL cholesterol, Ox-LDL: Oxidized LDL, PON1: Paraoxonase, TBARS: Thiobarbituric acid reactive substances, TC: Total cholesterol, TG: Triglyceride, VLDL-C: VLDL cholesterol

events. Direct visualization of Ox-LDL in the vessel wall would be an ideal marker to measure the risk of cardiovascular events and is an area of active study, but this approach is not currently feasible in humans. The use of Ox-LDL biomarkers, however, show promise in diagnosing pre-clinical atherosclerosis in symptomatic individuals, monitoring active disease and predicting cardiovascular outcomes (20).

Oxidative stress may cause plaque rupture in coronary heart disease (CHD) patients. The oxidative stress is likely to either induce or intensify the inflammatory action, and may act together with inflammatory factors to cause or accelerate plaque rupture (21). Our present findings show a greatly increased production of plasma TBARS, which is an indicator of lipid peroxidation, in CAD patients, consistent with the findings of Serdar et al. (22). In their study, plasma TBARS and the change in plasma TBARS levels (D-TBARS) were significantly elevated in parallel with increased stenosed vessel number. The basal value was subtracted from the 3 h value to obtain D-TBARS which represents the degree of oxidative modification (capacity for peroxidation). However, we could not find any significant differences in TBARS levels between CAD patient subgroups (23, 24). Some investigators have found a relationship between elevated plasma lipid peroxides and LDL oxidation and the severity of coronary lesions (25, 26). However, controversial data have also been obtained in patients with CAD (27-30). Mutlu-Turkoglu et al. (31) reported that although plasma TBARS levels were increased in patients with CAD, these values did not vary in patients grouped according to affected vessel number. In addition, there was no significant correlation between Duke scores, a parameter that defines the extent of coronary disease, and plasma TBARS levels.

PON1 has been suggested as the factor largely responsible for the antioxidant role of HDL (8). PON1 is an enzyme with three activities: paraoxonase, arylesterase and diazoxonase (32), and its activity is inversely related to the risk of CAD (33). In our study, serum PON1 activities in patients with CAD were found to be significantly lower than those in the healthy control group. In addition, in CAD patients with double- and triple-vessel disease, the serum PON1 activities were found to be significantly lower than in the healthy control group.

On the other hand, there was a strong negative correlation between PON1 and the severity of disease. In addition, there was a positive, but statistically insignificant, correlation between Ox-LDL levels and the severity of disease. However, the relationship between the extent of CAD and the level of oxidant and anti-oxidant markers is not well known. Although most studies have stated that PON1 activity was decreased in patients with CAD (22, 34, 35), studies on the relationship between PON1 activity and the extent of coronary stenosis are very limited (22, 35-38).

Paraoxonase is present in a distinct HDL subspecies containing ApoA1 and clusterin or apoliprotein J (apoJ) (39). La Du et al. (40) showed that it is extremely difficult to remove ApoA1 from PON1 during purification from human serum, which has led to the suggestion that ApoA1 and PON1 are closely associated. The average serum ApoA1 levels in healthy control groups were higher than those in the group of single-, double- and triple-vessel

CAD disease groups in this study. In addition, CAD patients with double-vessel disease were found to have significantly higher serum ApoA1 levels than CAD patients with triple-vessel disease. Rozek et al. (41) reported that in 91 male subjects with severe carotid artery disease and 184 control subjects, PON1 activity in the disease group was strongly correlated with LDL-C and VLDL-C in the absence of the expected HDL3 and ApoA1 associations. In the present study, however, we could not confirm their findings, possibly in part because of the different study design and the patient populations studied. Graner et al. (36) suggested that PON1 activity toward phenylacetate and PON1 concentrations are lower in subjects with significant CAD, and there is a significant relationship between activity and concentration of PON1 and the severity and extent of coronary atherosclerosis. The results show the relevance of PON1 activity and concentration for describing associations between atherosclerotic disease and the enzyme. More importantly, the study shows how the protective role of HDL could be modulated by its components such that equivalent serum concentrations of HDL-C may not equate with an equivalent potential protective capacity.

Conclusion

Our findings provide evidence that both elevated levels of serum Ox-LDL and reduced PON1 activity in CAD patients are associated with the severity of CAD and with the occurrence and number of obstructed vessels. This observation may assist in providing more information as to how the unbalanced antioxidant/oxidant equilibrium may predispose individuals to atherogenesis.

Study Limitations
The sample size of this study is too small to investigate the possible relationship between Ox-LDL, PON1 activity and TBARS levels in patients with angiographically defined CAD.

Conflict of Interest
No conflict of interest was declared by the authors.

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Author Contributions
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