

The Association of Lysyl oxidase G473A Polymorphism in Coronary Artery Ectasia

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Abstract

Coronary artery ectasia (CAE) is defined by a ≥ 1.5 -fold expansion coronary artery vessel diameter, with respect to the adjacent coronary artery vessel. Atherosclerosis and extracellular matrix changes are thought to play an important role in CAE development. Lysyl oxidase (LOX) is part of an important enzyme family involved in the regulation of connective tissue. LOX deficiency has been associated with aortic aneurysm, fold, and dissection. Our study aimed to investigate the relationship between LOX gene G473A (rs1800449) polymorphism and CAE. Eighty-eight patients diagnosed with CAE and 75 healthy individuals were included in the study. The CAE group demonstrated significantly higher hyperlipidemia ($p=0.01$), male sex incidence ($p=0.06$), serum TNF- α ($p=0.03$), and sE-selectin ($p=0.02$). The LOX genotype and allele distribution showed no significant difference between the groups. Notably, patients with CAE carrying the LOX-CT genotype demonstrated significantly higher TNF- α ($p=0.04$) and sP-selectin ($p=0.02$) levels than those carrying the LOX-CC genotype. Higher TNF- α values and hyperlipidemia were associated with the risk of CAE. Further, we observed that TNF- α levels were higher in patients with right coronary artery (RCA) ectasia. Additional large-scale studies to include other LOX gene polymorphisms may support our findings and further elucidate their relationship to CAE.

Full Text

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Tables

Table 1 The demographic, clinical and biochemical characteristics of the study groups

	Healty Controls (n=75)	CAE patients (n=88)	p value
Age(years)	60.65±11.2	61.99±10.1	0.43
Gender (female/male)	36/39	29/59	0.06
Hypertension (n,%)	33 (%44)	50 (%56.8)	0.12
Diabetes Mellitus (n/%)	25 (%33.3)	29 (%33)	0.95
Hyperlipidemia (n,%)	27 (%36)	51 (%58)	0.01
EF (%)	58.55±0.88	57.02±1.07	0.29
Glycose (mg/dl)	118.29±60.9	114.8±38.8	0.65
HbA1c (%)	6.17±0.9	6.33±1.1	0.37
BUN (mg/dl)	17.03±6.4	16.17±4.9	0.34
Creatinine (mg/dl)	0.86±0.25	0.92±0.27	0.14
TC (mg/dl)	181.23±42.2	184.06±41.5	0.67
HDL-C (mg/dl)	47.28±12.4	44.22±11.9	0.11
LDL-C (mg/dl)	125.23±36.2	126.86±41.2	0.79
TG (mg/dl)	137.09±72.4	173.35±103.06	0.01
ALT (SGPT) (U/L)	23.33±2.76	26.11±2.47	0.45
AST (SGOT) (U/L)	22.08±13.6	22.86±13.9	0.72
TSH (µu/ml)	2.51±0.32	2.26±0.21	0.50
INR	1.02±0.03	1.25±0.09	0.02
WBC (mm ³)	7931.82±372.93	8444.64±350.23	0.32
Hgb (gr/dl)	12.93±0.25	13.67±0.23	0.04
Hct (%)	38.78±0.76	40.94±0.69	0.04
Plt (mm ³)	249954.55±10487.38	39267.86±9152.15	0.44
Neutrophils (mm ³)	4843.18±279.39	4944.64±242.17	0.78
Lymphocytes (mm ³)	2293.18±133.35	2625.00±227.31	0.24

HbA1c, Hemoglobin A1c; TC, Total cholesterol; HDL-C, High density lipoprotein-cholesterol; LDL-C, Low density lipoprotein-cholesterol; TG, Triglyceride; ALT, Alanine aminotransferase; SGPT, Serum glutamic pyruvic transaminase; AST, Aspartate aminotransferase; HbA1c, Hemoglobin A1c; TC, Total cholesterol; HDL-C, High density lipoprotein-cholesterol; LDL-C, Low density lipoprotein-cholesterol; TG, Triglyceride; ALT, Alanine aminotransferase; SGPT, Serum glutamic pyruvic transaminase; AST, Aspartate aminotransferase; SGOT, Serum glutamic oxaloasetic transaminase; BUN, Blood urea nitrogen; TSH, Thyroid stimulatitng hormone; INR, International normalized ratio of prothrombin time; WBC, white blood cells; Hgb, Hemoglobin; Hct, Hemotocrit; Plt, Platelets; EF, injection fraction; n, number. The

difference between the groups was analyzed by student's *t* test for mean values (mean±SD), and chi-square (*x*²) test for values with percentage (%). Bold values of *p* < 0.05 indicate statistical significance.

Table 2 Inflammatory parameters of the study groups

	Healty Controls (n=75)	CAE patients (n=88)	<i>p</i> value
IL-33 (pg/ml)	20.37±10.4	46.3±13.4	0.18
IL-8 (pg/ml)	0.06±0.06	3.6±2.1	0.11
PAI-1 SERPIN (pg/ml)	5076±771	7006±762	0.09
GM-CSF (pg/ml)	6.6±5.4	10.9±5.35	0.59
TNF-α (pg/ml)	157.25±13.08	200.81±14.64	0.03
PECAM (pg/ml)	6652±1872.06	11468.26±1740.73	0.07
IL-6 (pg/ml)	10.07±2.01	10.52±2.67	0.91
sE selectin (pg/ml)	31164±4117.7	57159±10496.9	0.02
sP selectin (pg/ml)	17033±1787.5	22868±3471.63	0.14
IL-1β (pg/ml)	8.6±2.18	11.96±1.64	0.22

The difference between the groups was analyzed by student's *t* test for mean values (mean±SD), and chi-square (*x*²) test for values with percentage (%). Bold values of *p* < 0.05 indicate statistical significance.

Table 3 The genotype and allele distributions of the study groups

LOX rs1800449	Healty Controls (n=75)	CAE patients (n=88)	P value
Genotypes (n,%)			
CC	46 (61.3%)	59 (67%)	>0,05
CT	27 (36.0%)	26 (29.5%)	>0,05
TT	2 (2.7%)	3 (3.4%)	>0,05
Alleles			
C	119 (79.3%)	144 (81.8%)	>0,05
T	31 (20.7%)	32 (18.2%)	>0,05

n, number. The difference between the groups was analyzed by chi-square (*x*²) test. Bold values of *p* < 0.05 indicate statistical significance.

Table 4 The comparison of clinical and biochemical parameters according to LOX genotypes in the patient group.

CAE patients	CC Genotype (n=59)	CT Genotype (n=26)	TT Genotype (n=3)	P value
(mg/dl)	170.63±12.45	164.27±16.08	305.67±168.246	CC/TT: 0,03 CT/TT: 0,02
Γ (U/l)	22.08±1.62	35.50±7.21	24.0±9.53	CC/CT:0,01
Γ (U/l)	20.58±1.09	28.46±4.19	19.33±6.83	CC/CT:0,02
F-α (pg/ml)	183.21±18.42	244.46±25.80	164.32±33.33	CC/CT: 0,05
selectin (pg/ml)	17884.45±2535.14	35694.27±9367.62	10249.36±6144.20	CC/CT: 0,02

n, number. The difference between the groups was analyzed by student's *t* test for two group comparison (CC genotype vs T allele) and one way Anova test for three group comparison (among CC,CT and TT genotypes).

Table 5 Multivariate logistic regression analysis for the risk of coronary artery ectasia risk

Dependent variable	Independent variable	Exp(B) (OR)	p value	95 % CI
CAE	TNF-α	0.001	0.05	0.000 - 0.003
	TG	0.001	0.31	-0.001 - 0.002
	Hyperlipidemia	0.223	0.03	0.011- 0.434

Figures

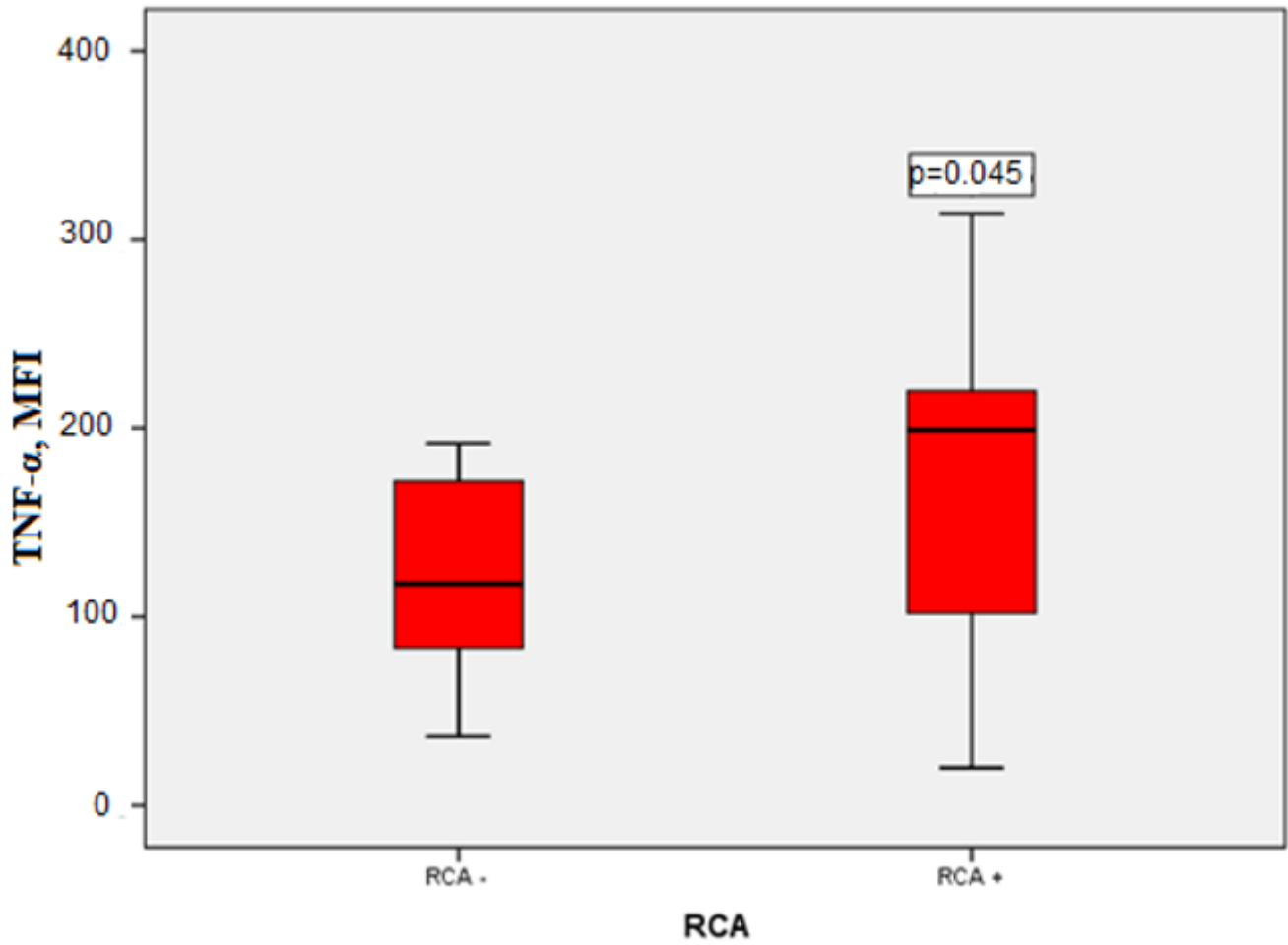


Figure 1

The comparison of serum TNF- α levels according to RCA* involvements in patients with CAE. *RCA, right coronary artery