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# LDL fatty acids composition as a risk biomarker of cardiovascular disease

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**Abstract** *Objective:* Fatty acid composition of Low-density lipoprotein (LDL) particle is an effective factor in LDL oxidation and atherosclerotic plaques formation. This study evaluates the relationship between LDL fatty acid composition and coronary artery disease (CAD).
*Methods:* 42 men with coronary artery disease (CAD-group) and 40 men without coronary artery disease (non-CAD-group) were selected. LDL fatty acid composition of blood samples was measured by gas chromatography.
*Results:* Ox-LDL was significantly high in CAD-group. Poly unsaturated fatty acids (PUFA) and PUFA/MUFA (Mono unsaturated fatty acids), linoleic acid and arachidonic acid were significantly higher in CAD-group than in non-CAD-group. In CAD-group, a reverse correlation was observed between oleic acid concentrations and ox-LDL levels and a direct correlation was seen between arachidonic acid concentrations and ox-LDL levels.
*Conclusion:* Composition of LDL is related to atherosclerosis and CAD. High levels of arachidonic and linoleic acids could increase LDL oxidation and atherosclerotic plaques formation. In addition, LDL arachidonic acid levels could be a better predictor of CAD.


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## Introduction

Low-density lipoprotein cholesterol (LDL) oxidation is a basic factor in atherosclerosis[1,2] and is affected by both endogenous and exogenous factors.[3] LDL fatty acid composition and particle size, antioxidants' level, phospholipase A2 activity and apoB100 are endogenous factors, which can play a role in LDL oxidation. Among the exogenous factors influencing LDL oxidation, we can refer to cellular peroxidation activity, oxidant, and antioxidant concentrations in extracellular fluid and plasma.[4–7] In addition, antioxidants, diets with a high intake of fruit and vegetables, high phenolic compound, statin therapy, and physical activity effects LDL oxidation rate and are able to protect LDL against oxidation.[8–10]

LDL fatty acid composition is an important factor in the LDL oxidation and formation of atherosclerosis. A high amount of poly unsaturated fatty acids (PUFAs), such as linoleic acid and arachidonic acid in LDL particles, can increase the susceptibility of LDL to oxidation.[11] Moreover, conjugated dienes formed during PUFAs oxidation can result in apoB100 modification.[12,13] High amounts of saturated (SFAs) and mono unsaturated (MUFAs) fatty acids, such as oleic acid, do not increase the susceptibility of LDL to oxidation.[1,2,14] Thus, it can be concluded that peroxidation of PUFAs in LDL particles may produce oxidized LDL (ox-LDL).[15] During lipid peroxidation process, unsaturated fatty acids (UFAs) are converted to lipid peroxide by free radicals or enzymatic reactions.[16,17] In the initiation phase, a hydrogen atom in a double bound of UFAs is diminished by initiating radicals, and then lipid peroxyl radical is formed rapidly during the addition of oxygen molecules to central carbon radicals. In propagation phase, lipid peroxide is formed during peroxyl lipid's radical attack on other PUFAs. Then, two peroxyl radicals can react with each other and form a non-radical product in termination phase.[16,18] Therefore, during LDL oxidation and hydro peroxides decomposition, aldehydes are produced and apoB100 is chemically and structurally modified.[7,13,19]

Ox-LDL causes atherosclerosis, coronary artery disease, and cardiovascular disease in various forms, including cytotoxic effect on endothelial cells, chemo attractant effect on monocytes–macrophages, inhibitory effect on nitric oxide releasing, stimulating effect on smooth muscles cells proliferation, inhibitory effect on endothelial cell immigration, and stimulating effect on adhesion and aggregation of platelets. All of these changes can result in the formation of atherosclerotic plaques.[10,20,21] Furthermore, formation of antibodies against modified LDL (ox-LDL and modified apoB100) and immune complexes are the key stages in atherosclerosis pathogenesis.[22] Ox-LDL, containing modified apoB100, is taken by scavenger receptors on the surface of monocytes–macrophages in sub endothelial spaces. Ox-LDL aggregations in monocytes–macrophages cells convert monocytes–macrophages cells to foam cells. These processes cause initiation of atherosclerotic plaques and formation of injuries in coronary arteries.[7,16,23] In vitro condition, copper ions can cause oxidation of lipoproteins so this oxidation of lipoprotein mimics the in vivo conditions of lipid peroxidation.

Because of the increasing trend of cardiovascular mortality, and high prevalence of these diseases in our country, this study was performed to elucidate relationship between LDL fatty acid composition and risk of coronary artery disease (CAD).

## Materials and methods

### Subjects

In this research, 82 men, aged 40–60, with chest pain and without any CAD risk factors (body mass index (BMI) between 18.5 and 24.9 $kg/m^2$, nonsmoker, normolipidemic, and non-diabetic) were selected with simple sampling method from Cat lab of Chamran hospital, and were divided into two groups of CAD and non-CAD. The exclusion criteria included renal disease, malignant disease, familial hypercholesterolemia, thyroid disease, myocardial infarction or coronary artery bypass grafting (CABG) 6 weeks prior to angiography, alcohol consumption, lipid lowering medication and any kind of drugs interfering with lipid metabolism (such as corticosteroid, tiazid, lipid decreasing drugs).[17]

Patients with at least 70% stenosis in one or more major epicardial arteries were selected as CAD group ($n = 42$), and subjects with no evidences for stenosis in their major coronary arteries were considered as members of the non-CAD group ($n = 40$).

Demographic information about lifestyle, medication, and family history were acquired through interviews with subjects, and they signed the informal consent form. The Ethics Committee of Isfahan Cardiovascular Research Center approved this research.

### Measurement of clinical and anthropometric factors

At first, for each subject, a questionnaire was completed. Anthropometric factors such as weight and height were measured without shoes, in light clothes and by seca scale, and waist and hip circumferences were measured by a tape measure. Using a sphygmomanometer, systolic and diastolic blood pressures (clinical factors) were measured three times for each patient. BMI was calculated according to weight (kg)/height$^2$ ($m^2$) formula and waist–hip ratio (WHR) was also calculated.[20]

### Blood sampling and biochemical measurement

12–14 h fasting blood samples were taken to measure serum levels of fasting blood sugar (FBS/FBG), total cholesterol (T.C), triglyceride (TG), high density lipoprotein cholesterol (HDL), LDL, and etc. Automated enzymatic assay by Pars Azmoon kits (Tehran, Iran) and auto-analyzer Hitachi 902 (Hitachi, Tokyo, Japan) and special kits (Diagnosis Inc., Holzheim, Germany) was utilized to assess the mentioned factors.