

# The Role of Oxidized LDL in the Metabolic Syndrome

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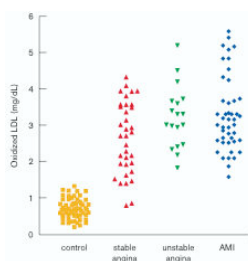
*The Metabolic Syndrome has become an epidemic, causing enormous health and life-threatening problems for patients worldwide. Several studies have shown a clear relationship between the Metabolic Syndrome and high levels of oxidized LDL, suggesting oxidized LDL to be a useful marker for the condition. Intervention studies have been successful in preventing the Metabolic Syndrome in parallel with lowering oxidized LDL levels. These studies have been too small to determine causality. Large prospective studies are needed to further elucidate the role of oxidized LDL in prevention of the Metabolic Syndrome.*

## Background

The Metabolic Syndrome is a cluster of cardiovascular risk factors that includes obesity, dyslipidemia, hypertension and insulin resistance. Each of these risk factors can shorten one's life due to their individual roles in accelerating atherosclerosis, giving rise to several life threatening complications. These conditions constitute some of the main risk factors for diabetes and cardiovascular disease.

This clustering of risk factors is becoming a major epidemic (paralleling obesity and diabetes) and contributes to the leading cause of morbidity and mortality in the western world. The prevalence of obesity and diabetes is rapidly increasing. More than 50% of Europeans are classified as overweight and every year 7 million new cases of diabetes are diagnosed. Diabetes is most prevalent in developing countries, placing a tremendous economic burden on these populations (Diabetes Atlas, 2007).

An alarming increase in cardiovascular disease prevalence is projected to occur due to population ageing, unhealthy diets, body fatness and sedentary lifestyles. These facts call for increased research, use of predictive markers and identification of optimal interventions. Oxidation of LDL is central to current theories of atherosclerosis. Mercodia Oxidized LDL ELISA assays have been used in numerous studies to predict atherosclerosis and may be a useful tool in assessing Metabolic Syndrome risk.



**Figure 1.** Compared to controls, oxidized LDL levels are elevated in patients with stable angina, unstable angina and acute myocardial infarction (AMI). Published data by Holvoet *et al.* (1998).

## Oxidized LDL & Metabolic Syndrome

Atherosclerosis is considered to be an inflammatory disease. During inflammation a variety of cells produce inflammatory mediators (e.g., oxidants) as defenses against disease-causing substances. Unlike native (unmodified) LDL that lacks inflammatory properties, oxidized LDL (ox-LDL) is an emerging risk factor that activates circulating monocytes and stimulates their ability to infiltrate the vascular wall. The resulting inflammation is a primary stage in atherogenesis and common in the metabolic syndrome (Cipolletta *et al.* 2005).

Holvoet *et al.*, 2007, have shown that the prevalence of cardiovascular disease is higher in individuals with the metabolic syndrome or with higher levels of ox-LDL. The highest prevalence was found in persons with the Metabolic Syndrome combined with elevated ox-LDL (figure 2). Sigurdardottir *et al.*, 2002, found that the Metabolic Syndrome was accompanied by high plasma ox-LDL concentrations compared with those without the syndrome. Moreover they found that ox-LDL levels were associated with most of the risk factors constituting the Metabolic Syndrome and was, in addition related to small LDL particle size.

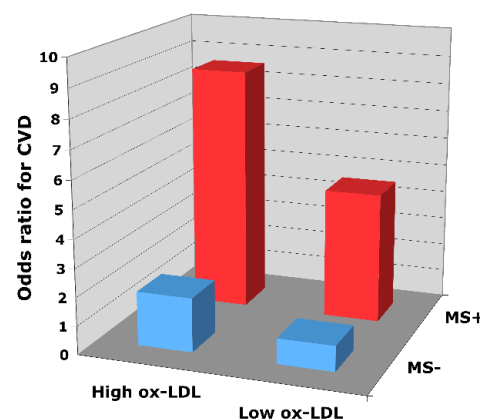
Furthermore, the Cardiovascular Risk Development In young Adults (CARDIA) study showed that elevated ox-LDL but not elevated LDL cholesterol was associated with a higher risk of future Metabolic Syndrome (Holvoet *et al.* 2008).

These findings suggest that any interventions that succeed in lowering the levels of ox-LDL may also ameliorate the effects of the Metabolic Syndrome.

So far, lifestyle and therapeutic interventions have been proposed as a key to success. Studies suggest that a gluten-free vegan diet (Elkan *et al.* 2008) reduces concentrations of ox-LDL. Similar results were seen with grape juice and vitamin E supplementation (Castilla *et al.* 2008). These studies have been too small to determine causality. However, they confirm other findings that suggest antioxidant supplementation is effective in lowering ox-LDL. Among those, Verreth *et al.*, 2004, showing that decreased deposition of ox-LDL occurred due to improved balance between pro-oxidant and antioxidant enzymes in adipose tissue.

In a study by Tjonna *et al.*, 2008, high intensity exercise training was highly beneficial in preventing the metabolic syndrome as well as reducing ox-LDL levels.

According to current studies, monitoring ox-LDL levels may be useful in cardiovascular risk stratification of patients with the Metabolic Syndrome.



**Figure 2.** Prevalence of cardiovascular disease according to the presence of the Metabolic Syndrome and high oxidized LDL. Published by Holvoet *et al.* 2007.

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