Small dense LDL in Patients with Prediabetes and Type 2 Diabetes: It's Significance for the Development of Diabetes and Atherosclerosis

Summary / Zusammenfassung

LDL size, diabetes and the metabolic syndrome: The worldwide incidence of type 2 diabetes mellitus is increasing and accounting for 6-12% of total health care expenditure in industrialized countries (1). Hypertriglyceridemia, low HDL and increased fraction of small dense LDL particles are frequent lipid abnormalities in insulin resistance and type 2 diabetes mellitus (2-4) and are associated with increased cardiovascular mortality (5, 6). An association of LDL particle size with the cluster of risk factors that characterize the insulin resistance syndrome has also been demonstrated (7) and there is strong evidence that the smaller denser LDL particles can be added to the group of changes described as syndrome X, also called the metabolic syndrome (3, 8). In a nested case control study of 204 elderly men and women from Finland, it has been demonstrated that subjects with predominance of small dense LDL had a greater than two fold increased risk for developing type 2 diabetes mellitus over a 3.5 year follow up period, independent from age, sex, glucose tolerance and body mass index. Importantly, every increase of 5Å in LDL diameter was associated with a 16% decrease in risk of developing type 2 diabetes mellitus (9).

LDL size and intima media thickness (IMT): Hulthe et al. (10) assessed the prevalence of metabolic syndrome in a population-based sample of clinically 58 years old healthy men, using the WHO definition (11). The authors found that LDL size was significantly smaller in subjects with the metabolic syndrome, in relation to those without it. Subjects with decreased LDL size had a higher prevalence of moderate to large plaques in the carotid artery compared with subjects with pattern A. Interestingly, decreasing LDL peak particle size was significantly associated with increasing IMT of the common carotid artery, the carotid artery bulb, and the common femoral artery. There was a statistically significant association between plaque occurrence and size and the LDL peak particle diameter in both the carotid and femoral arteries.

LDL size and endothelial dysfunction: Small dense LDL may contribute significantly to endothelial dysfunction: Endothelial dysfunction is frequently observed with other features of insulin resistance, such as the presence of small dense low-density lipoprotein particles. Importantly, this association is independent of other causes of endothelial dysfunction such as LDL cholesterol, hypertension, and smoking. Endothelium-dependent vasodilatation in the brachial artery in subjects with type 1 diabetes was directly related LDL particle size and the authors suggested that LDL size may be a determinants of conduit and resistance vessel endothelial vasodilator function. Interestingly, in men with diabetes type 2 small dense LDL particle size were associated with abnormal endogenous release of nitric oxide. Taken together the present literature suggests that ALP and particularly small dense LDL are significant contributors to endothelial dysfunction and small vessel disease.

Oral glucose testing can be used as a diagnostic test for diabetes (particularly during pregnancy). However, as a measure of impaired glucose tolerance it is a precious research tool which has also been used in large population based studies, including patients with diabetes. The term prediabetes is used when fasting blood glucose is between 5.6 and 7 mmol/l. It is associated with increased risk for diabetes and part of the metabolic syndrome.

The present study investigates the associations of LDL particle size in patients with prediabetes and diabetes with direct markers of atherosclerosis such as IMT, traditional plasma lipid, endothelial dysfunction and glucose tolerance in a 6 year prospective, observational study.
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