

Oxidative modification of HDL Apolipoprotein A-I and Apolipoprotein C-I Reveal Advanced Atherosclerotic Diseases

Abstract

High density lipoprotein (HDL) has been known to be able to protect vessels from atherosclerotic changes. The anti-atherosclerotic property of HDL comes mainly from the reverse cholesterol transport (RCT) effect, a process delivering vascular cholesterol to liver for excretion. ApoA1 is the major protein of HDL. It is composed of 2 dimers linked by disulfide bond with a molecular weight around 28 KDa. ApoA1 can promote RCT by either accepting cholesterol from extrahepatic tissue or acting as a co-factor of LCAT. In addition to RCT. ApoA1 also possess anti-inflammation, anti-oxidation, and anti-thrombosis properties. ApoA1 can inhibit LDL oxidation, prevent cytokine-induced adhesion molecular formation, stabilize prostacyclin, and enhance nitric oxide formation. The modification of apoA1 either enzymatic or non-enzymatic, such as glycation, carbamylation, or oxidation, can compromise ApoA1 function and makes HDL proatherogenic. Apolipoprotein C1 (ApoC1) is another HDL lipoprotein important for RCT. ApoC1 has several functions and is implicated in the regulation of several lipase enzymes. By acting as a cofactor of LCAT, ApoC1 plays a role in exchange of esterified cholesterol between lipoprotein and in the removal of tissue cholesterol. Modification of ApoC1 may have adverse impact on atherosclerotic diseases.

In this study, HDL of patients with known risk of atherosclerosis such as diabetes, uremia, and hyperlipidemia subjects were studied using Tris-Bis gradient gel, MALDI-TOF and nanoLC-MS/MS approaches. The results showed that patients with advanced atherosclerosis have higher degree of oxidative ApoA1 and oxidation of ApoC1 than those without frank atherosclerosis. In the patients with advanced atherosclerosis, ApoA1 showed significantly separated bands on Tris-Bis gel compared to single band presented on SDS PAGE. The preliminary results showed the detection of oxidative ApoC1 by MALDI-TOF and the observation of separated bands on Tris-Bis gel could be potential diagnosis methods to predict the risk of advanced atherosclerosis.