Hyperlipidemia and Cardiovascular Disease: Clinical Challenges in IT Era

Title: The Controversy of Triglyceride and Atherosclerosis

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The relationship between cholesterol and atherosclerosis has been known for a long time, and studies on familial hypercholesterolemia have elucidated the relationship at the molecular level. Many large-scale clinical studies have also established this relationship. In contrast, no consistent view of the relationship between triglyceride (TG) and atherosclerosis has been reached. It is not reported that patients with type I hyperlipidemia with increased chylomicrons and type V hyperlipidemia with increased chylomicrons and VLDL are likely to develop atherosclerosis. The relationship of type III hyperlipidemia with increased VLDL remnants, type IIb with increased LDL and VLDL, and familial combined hyperlipidemia with atherosclerosis is well established. It is also well known that diabetes and metabolic syndrome are often accompanied by hypertriglyceridemia and related to atherosclerosis. Although there is no doubt that hypertriglyceridemia and atherosclerosis are closely related, hypertriglyceridemia has not been established as an independent risk factor, and reasons for this include the diversity of the pathology of hypertriglyceridemia and close association with abnormal lipid metabolism, such as low HDL cholesterolemia, and emergence of small dense LDL and VLDL remnants. Chylomicrons, VLDL, and VLDL remnants are pathological conditions of increased TG or neutral fat. What then is the difference? Lipoprotein lipase hydrolyzes TG in TG-rich chylomicrons and VLDL to free fatty acids, slowly metabolizing them to their remnants, and VLDL is metabolized to LDL. In types I and V hyperlipidemia, metabolism to remnants does not occur because lipoprotein lipase is inactive. In a pathology of excess inflow of accumulated visceral fat as free fatty acids into the liver via the portal vein, such as the pathology of metabolic syndrome, the production of TG-rich VLDL is induced in the liver, and TG-rich VLDL is released into the circulation. In this syndrome, the lipoprotein lipase activity is reduced due to insulin resistance, and metabolism of TG-rich VLDL delays, resulting in increases in TG-rich VLDL remnants and small dense LDL. HDL production is also reduced at the same time. Macrophages incorporate TG-rich remnants and become foam cells, forming the central pathology of atherosclerosis. Small dense LDL is easily oxidized and creates conditions under which oxidized LDL is likely to be formed. A low blood HDL level may also play a role in the formation of atherosclerosis. In addition to these basic study results, as clinical results, Helsinki Heart, BIP, and BECAIT studies demonstrated that administration of fibrates to patients with this pathology decreased the production of TG-rich VLDL and TG-rich VLDL remnants, and reduced the incidence of atherosclerotic coronary arterial disease. In this report, the current trend is outlined based on these findings.