



Enhanced Intestinal Absorption of Cholesterol along with Increased Chylomicron Remnants for De novo Progression of Coronary Stenosis

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Serum concentrations of low-density lipoprotein (LDL) cholesterol and total cholesterol (TC) are influenced by cholesterol production from the liver and cholesterol absorption in the intestine. As shown in an epidemiological study, both decreased cholesterol synthesis and increased cholesterol absorption in the intestine are significant and independent predictors of prevalent coronary heart disease (CHD) relative to established coronary risk factors¹. Patients with hyper-LDL cholesterolemia are usually treated using statins for the prevention of CHD, and the long-term use of statins enhances the cholesterol absorption in the intestine by the feedback inhibition of cholesterol production by the liver. An increased cholesterol content in intestinal epithelial cells may cause increased production of chylomicron (CM), resulting in hypertriglyceridemia and the accumulation of CM remnants in the postprandial sera (Fig. 1). Similar to small, dense LDL or very-low-density lipoprotein remnants, CM remnants are related to atherogenicity by enhancing systemic inflammation, platelet activation, coagulation, thrombus formation, and macrophage foam cell formation². Concentration of the fasting apolipoprotein (apo)B-48, which is a quantitative marker for CM remnants³, correlates with carotid intima-media thickening⁴ and the prevalence of chronic⁵ and new-onset coronary artery disease (CAD)⁶. Therefore, both the increased intestinal cholesterol absorption and the accumulation of CM remnants are considered to be

high-risk status for CHD events in the statin treatment; however, it is unclear whether these markers were also useful for the prognosis of coronary events for secondary prevention.

Recently, percutaneous coronary intervention (PCI), including stenting, has been established as a standardized treatment for improving angina and activity of daily life in Japanese patients with CHD. The importance of cholesterol-lowering therapy, including high-dose statin therapy, in patients with CHD has been long emphasized. It was shown that aggressive lipid-lowering therapy is at least as effective as PCI in reducing CHD events in patients with hyper-LDL cholesterolemia and mild coronary stenosis (asymptomatic or mild-to-moderate angina)⁷. On the other hand, the correlation between the accumulation of remnant lipoproteins and the development of coronary stenosis is not known. Moreover, coronary stenosis after PCI involves de novo stenosis and in-stent restenosis after the stenting of drug-eluting stents or bare-metal stents, and there is no data on which kind of coronary stenosis is correlated with the accumulation of CM remnants. If we can truly understand these correlations, we can develop useful strategies for the prevention of coronary stenosis in relation to the atherogenic characteristics of the impaired lipid metabolism.

In the current study, Mori *et al.* examined the importance of enhanced cholesterol absorption in the intestine and the accumulation of CM remnants in sera for the development of coronary stenosis⁸. They found that cholesterol absorption marker (campesterol/TC and campesterol/lathosterol ratio) and apoB-48 concentration were elevated in patients with CHD compared with patients who did not have CHD even though their serum LDL cholesterol levels were controlled using statins, suggesting that these two metabolic changes were important for de novo prognosis of

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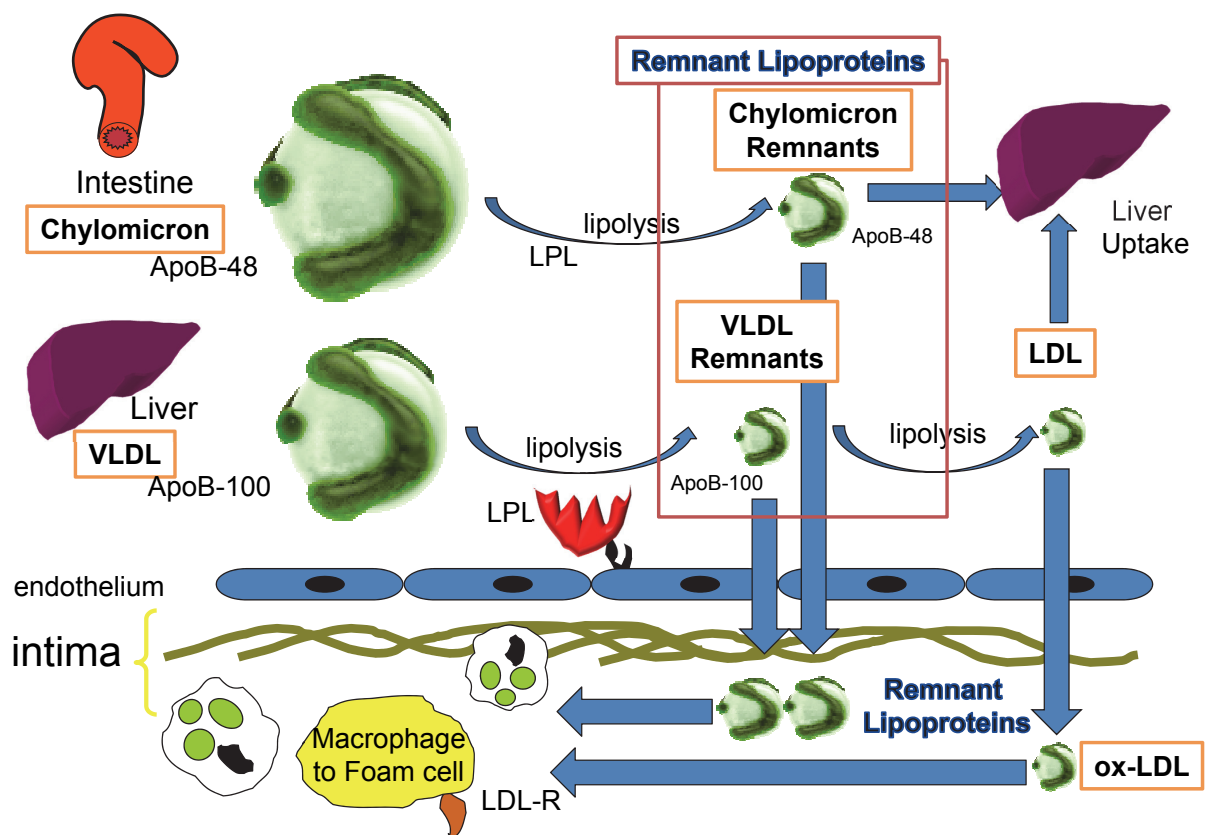


Fig. 1. Remnant Lipoproteins from Exogenous and Endogenous Pathways

Intestine-derived chylomicrons are metabolized into chylomicron remnants by the lipoprotein lipase (LPL) and liver-derived Very-Low Density Lipoproteins (VLDLs) are into VLDL remnants. These two kinds of remnant particles are able to enter the subendothelial space directly and accelerate the macrophage foam-cell formation as well as oxidized-low-density lipoproteins (ox-LDLs).

coronary stenosis. Moreover, in patients who already received PCI, the prognosis with regard to whether they would show “in-stent restenosis” at stented segments or “de novo progression” other than stented segments is important for future strategy for preventing secondary coronary events. Because high campesterol/TC and apoB-48 concentrations were associated with de novo lesion progression after PCI but not with in-stent restenosis, Mori *et al.* clearly showed that the increases in intestinal cholesterol absorption and the accumulation of CM remnants enhance the progression of de novo coronary stenosis. This study is valuable as it explicitly demonstrates that residual risk factors, such as enhanced cholesterol absorption and accumulation of CM remnants, are important for the de novo synthesis of coronary stenosis with and without previous PCI even though their hyper-LDL cholesterolemia were properly treated using statins.

Conflict of Interest

None.

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