HDL3 Cholesterol Levels in an Elderly Population

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Editorial

HDL$_3$ Cholesterol Levels in an Elderly Population

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The HDL hypothesis was almost negated by three negative results of three low-molecular-weight chemical CETP inhibitors in the phase 3 trials, although low CETP activity, high levels of large HDL (i.e., HDL$_2$), and decrease in coronary artery disease prevalence have been demonstrated in genetic epidemiological studies of several SNPs[1)]. However, there are still hopes for the revival of the HDL hypothesis. One has not been well tested whether or not enhanced lipoprotein lipase activity, TG lipolysis, and enhanced HDL synthesis, i.e., VLDL-HDL pathway hypothesis is anti-atherogenic[2)]. The other is cellular cholesterol efflux and small HDL (i.e., HDL$_3$) hypothesis[3)].

HDL consists of heterogeneous particles in terms of density (1.063–1.21 g/mL) and has an apolipoprotein composition of apoA-I, apoA-II, apoCs, and apoE and lipid composition of FC, CE, TG, and PL. Recent studies have suggested that specific lipids, such as sphingomyelin, ceramide, and sphingosine-1-phosphate (S-1-P), may play a key role in the HDL' s functions[4)]. S-1-P receptors are coupled with G proteins, thereby stimulating cellular migration and proliferation and modulating vascular tonus, inflammation, and a barrier function between cells. S-1-P is rich in dense HDL[5)]. Therefore, HDL$_3$ levels may act as S-1-P carriers, playing a specific role in vascular protection.

The current study by Dr. Notsu *et al.* investigated the association between HDL subclasses and carotid intima-media thickness in the Shimane CoHRE Study conducted in the Oki Island in the Japan Sea[6)]. HDL$_3$ cholesterol is negatively associated with age both in men and women. Simple correlation showed that max-IMT has an inverse relation with HDL$_3$ cholesterol levels, but multivariate analyses negated the association when age was included. One explanation for this finding is age acting as a confounding factor associated with both low HDL$_3$ cholesterol and increased carotid atherosclerosis (**Fig. 1**).

In terms of the future direction of HDL research, it would be interesting to examine whether or not low HDL$_3$ phenotype related with sedentary life could be corrected by enhancing ABCA1 or LPL activity through dietary and physical activity instruction or drug therapy.

Conflict of Interest

None.

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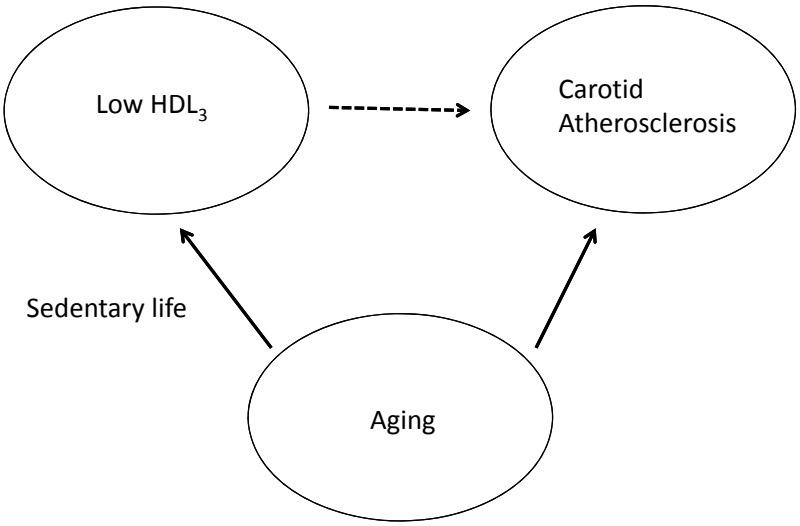

Fig. 1. Clinical significance of HDL3 cholesterol levels

Low HDL3 cholesterol is correlated with carotid atherosclerosis, but it is not causal. Aging may be a confounding factor between HDL3 cholesterol and carotid atherosclerosis.

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