Editorial Comment

Low-Density Lipoprotein Subfraction as a New Risk Factor for Silent Cerebral Infarction in Hypertensive Patients

Satoshi HOSHIDE[1] and Kazuomi KARIO[1]

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Silent cerebral infarction (SCI) is sometimes detected incidentally by magnetic resonance imaging in patients who demonstrate no localized neurological symptoms of stroke. In elderly patients, SCI has been associated with fall (*1*), as well as with cognitive dysfunction and dementia (*2*). Prospective studies have reported that the incidence of SCI is now 5- to 10-times greater than the incidence of symptomatic stroke (*3*, *4*).

Age and hypertension are the most important risk factors for SCI, and thus elderly hypertensive patients are at especially high risk for the disease (*5*–*12*). Previous studies have reported that elderly hypertensive patients who show an abnormal pattern of diurnal blood pressure (BP) variation—including both non-dippers, who show a diminished nocturnal BP fall, and extreme-dippers, who have a marked nocturnal BP fall—also have an increased risk of SCI (*5*, *6*). In regard to other cerebrovascular risk factors, it has been reported that insulin resistance (*8*), diabetes mellitus (*9*) and lipoprotein(a) (*7*) are all associated with SCI in hypertensive patients. However, the relation between hyperlipidemia and SCI has not been clarified. Kato *et al*. recently reported that LDL-3, one of the low-density lipoprotein (LDL) subfraction levels, is a risk factor for SCI in hypertensives (*13*).

The white matter and basal ganglia are the most frequently affected areas in SCI. The pathogenesis of SCI has been considered to differ between the white matter infarction and the basal ganglia infarction, and there is a difference in risk factors between these two types of SCI (*14*, *15*). The SCI in the white matter might be associated with age and hypertension, while that in the basal ganglia might be paralleled by subclinical systemic atherosclerosis, which also partly determines of the development of coronary atherosclerosis. Kato *et al*. reported that LDL-3 was more strongly associated with the SCI in the basal ganglia than with that in the white matter (*13*).

In a recent study, the LDL particle size was shown to be more strongly correlated with the pathogenesis of atherosclerosis than with the LDL cholesterol level (*16*). However, the measurement of LDL particle size is too laborious for general clinical use, whereas LDL-3 measurement can be performed simply. Small dense LDL particles show greater susceptibility to oxidative modification than typical LDL particles *in vitro*. The oxidative LDL has been strongly associated with the progression of atherosclerosis (*17*). Systematic atherosclerosis progressed by oxidative LDL might be independently involved in the pathologic process of SCI. It has been demonstrated that LDL-3 was highly atherogenic and associated with coronary artery disease; however, the relationship between LDL-3 and cerebrovascular disease remains unclear. Kato *et al*. proved that atherosclerosis plays a major pathogenic role in SCI in the basal ganglia. LDL-3 might play an important role in the relationship between cardiovascular and cerebrovascular disease.

From the [1]Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, Shimotsuke, Japan.

Address for Reprints: Kazuomi Kario, M.D., COE (Center of Excellence) Program, Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, 3311–1, Yakushiji, Shimotsuke 329–0498, Japan. E-mail: kkario@jichi.ac.jp

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