Dietary and Physiological Factors Affecting Lipid Metabolism and Cardiovascular Risk

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Summary Atherosclerotic cardiovascular disease (ASCVD) is one of the leading causes of death worldwide. The risk of developing CVD is associated with an unhealthy lifestyle. A high level of low-density lipoprotein (LDL) cholesterol (LDL-C) is a primary risk factor for ASCVD. However, even if the LDL-C management target has been achieved, hypertriglyceridemia and a high level of total cholesterol minus high-density lipoprotein (HDL) cholesterol (non-HDL-C), which contains cholesterol concentrations of triglyceride-rich lipoproteins, are considered a significant residual risk factor for ASCVD and consequently the management of these conditions is important for controlling the residual risk for ASCVD.

Key Words ASCVD, HDL, LDL, n-3 fatty acids, triglyceride

As reported by the World Health Organization (WHO), atherosclerotic cardiovascular disease (ASCVD) is cited in the 10 leading causes of death worldwide (1). The risk of developing ASCVD is associated with an unhealthy lifestyle, diet and other factors. A high level of low-density lipoprotein (LDL) cholesterol (LDL-C) is a primary risk factor for ASCVD. However, even if the LDL-C management target has been achieved, hypertriglyceridemia and a high level of total cholesterol (TC) minus high-density lipoprotein (HDL) cholesterol (non-HDL-C), which contains cholesterol concentrations of triglyceride (TG)-rich lipoproteins, are considered a significant residual risk factor for ASCVD and consequently the management of these conditions is important for controlling the residual risk for ASCVD (2–4).

The excessive intake of cholesterol and saturated fatty acids results in increased serum LDL-C levels. Excessive total energy intake and insufficient physical activity are the primary causes of metabolic syndrome, inducing the accumulation of visceral fat, increased TG levels (fasting and/or non-fasting hypertriglyceridemia), and decreased HDL-C levels. For example, adhering to the traditional Japanese dietary pattern with a low salt intake can help improve dyslipidemia and prevent ASCVD (2, 5–8). Moderate hypertriglyceridemia (TG 200–499 mg/dL) and more severe TG elevations (TG ≥500 mg/dL) are becoming increasingly prevalent in developed countries, likely driven in large part by growing rates of obesity and diabetes mellitus. The traditional Japanese diet is rich in n-3 fatty acids derived from fish oil, which is recommended for reducing serum TG levels in patients with hypertriglyceridemia (2–4, 9). However, recently, two double-blind, large-scaled, randomized controlled trials [REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial) and STRENGTH (Long-Term Outcomes Study to Assess Statin Residual Risk with Epanova in High Cardiovascular Risk Patients with Hypertriglyceridemia)] have shown contrasting results for the effect of high-dose, purified n-3 fatty acids for TG lowering on the prevention of ASCVD (10, 11). This issue is of high clinical relevance, given the uncertainty of the diverging results from these two large-scaled studies and the question whether n-3 fatty acids should be recommended as an adjunct to optimal guideline-based therapy for the prevention of ASCVD in patients with hypertriglyceridemia.

In addition, recently, the n-3 fatty acid index and eicosapentaenoic acid/arachidonic acid ratio has been drawing attention for the prevention of hypertriglyceridemia and ASCVDs (12–14). Harris et al. reported that risk for death from all causes was significantly lower in the highest vs the lowest quintile for circulating n-3 fatty acids after multivariable adjustment for relevant risk factors in a pooled analysis from 17 prospective studies (15).

A low HDL-C often occurs when serum TG level is high. The low HDL-C is an ASCVD risk factor as well as hypertriglyceridemia, but patients with extremely high HDL-C levels are also at a high risk for ASCVD (16). Over the recent decade, HDL dysfunction determination is more important for ASCVD risk control than HDL-C level (17, 18). Namely, the HDL determination method is changing from quantification (HDL-C) to qualification (HDL cholesterol efflux capacity) to do the exact risk evaluation (19, 20). Nutritional intervention methods for improving HDL function may also be helpful for the prevention of ASCVD.

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