Which Nutritional Factors Are Good for HDL?

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\textbf{To the Editor}

High-density lipoprotein (HDL) is a lipoprotein which has anti-atherogenic property by reversing cholesterol transport from the peripheral tissues to liver. Low HDL-cholesterol (HDL-C) as well as high LDL-C is associated with the development of coronary heart diseases \cite{1, 2}. Low HDL-C is commonly observed in patients with insulin resistance, obesity, and type 2 diabetes. In our previous study \cite{3}, serum HDL-C in type 2 diabetes \cite{4}, especially in type 2 diabetic patients with obesity \cite{5}, was lower than young lean men \cite{6} and low Framingham risk score subjects \cite{7} (Fig. 1), suggesting a significant influence of obesity, type 2 diabetes and insulin resistance on serum HDL-C levels.

Abnormal lipid metabolism induced by obesity, insulin resistance and type 2 diabetes was shown in Figure 2. Insulin resistance increases activity and expression of hormone-sensitive lipase (HSL) in adipose tissue, which catalyzes the breakdown of triglyceride (TG), releasing free fatty acids (FFAs) (Fig. 2) \cite{8}. Increased FFA entry to liver elevates hepatic production of very low-density lipoprotein (VLDL) which is a TG-rich lipoprotein. Insulin resistance also decreases the activity of lipoprotein lipase (LPL), the rate-limiting enzyme of the catabolism of TG-rich lipoproteins such as VLDL \cite{9}. The formation of HDL is related with the catabolism of TG-rich lipoproteins by LPL \cite{10}. Therefore, reduced LPL activity increases VLDL and reduces HDL.

Insulin resistance is associated with diminished LDL-receptor (LDL-R) \cite{11}, and intestinal mRNA expression of Niemann-Pick C1-like 1 (NPC1L1) protein is increased in diabetes \cite{12}, suggesting that insulin resistance and diabetes may increase serum LDL-C by reducing clearance and enhancing cholesterol absorption.

The dietary and nutritional factors could influence on HDL metabolism. To make “Dietary Reference Intake for Japanese 2020 (for low HDL-C)”, we searched meta-analyses of randomized controlled trials (RCTs) which investigated effects of energy and carbohydrate intake \cite{13}, glycemic index and intake of dietary fiber \cite{14}, intake of soy and non-soy legume \cite{15} and consumption of various fatty acids \cite{16}, on serum HDL-C levels. Seen in Figure 2, since low HDL-C is likely to accompany with obesity, insulin resistance and high TG. Elevation of LDL-C can accompany with low HDL-C; moreover, atherogenic properties of LDL such as small dense LDL, oxidized LDL and glycation of LDL are observed in type 2 diabetes \cite{17}. Therefore, we investigated effects of nutritional factors on metabolic parameters other than HDL-C such as LDL-C, TG, body weight and waist circumference.

The summary of effects of nutritional factors on HDL-C and other metabolic parameters was shown in Table 1. Low carbohydrate diet increased HDL-C and decreased TG, however, increased LDL-C. Dietary fiber consumption did not affect HDL-C and TG, however, reduced LDL-C. Soy consumption increased HDL-C and deceased both TG and LDL-C. Saturated fatty acid consumption increased HDL-C, however, also increased LDL-C. Industrially produced trans fatty acid consumption reduced HDL-C and increased LDL-C.

When we consider effects of nutritional factors on HDL-C to prevent atherosclerosis, we should think about effects of nutritional factors on other lipids, especially LDL-C.

\textbf{Conflict of Interest}

The authors declare that they have no conflict of interest concerning this article.

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Figure 1. Serum HDL-C levels in young men, middle-aged people with low Framingham risk score, type 2 diabetic patients without obesity and type 2 diabetic patients with obesity. This figure was made by modification of data in our previous report [3].

Figure 2. Abnormal lipid metabolism induced by obesity, insulin resistance and type 2 diabetes. FFA: free fatty acid; gLDL: glycated LDL; HSL: hormone-sensitive lipase; LDL-R: LDL-receptor; LPL: lipoprotein lipase; NPC1L1: Niemann-Pick C1-like 1; oLDL: oxidized LDL; sdLDL: small dense LDL; VLDL: very low-density lipoprotein.
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### Table 1. Effects of Nutritional Factors on HDL-C and Other Metabolic Parameters

|                      | HDL-C | LDL-C | TG     | BW, BMI, WC |
|----------------------|-------|-------|--------|-------------|
| **Carbohydrate**     |       |       |        |             |
| Low LC diets (versus LF diets) | ↑   | ↑   | ↓      | ↓           |
| Low LC diets         | ↑     | →    | ↓      | ↓ or →      |
| Low GI diets         | ↑ or →| ↓ or →| ↓ or →| BW → or BMI → or WC → |
| Free sugars          | ↑     | ↑    | ↑      | →           |
| Fructose (hypercaloric) | →  |     | ↑      |             |
| Fructose (isocaloric) | →    | → or ↑| →      |             |
| **Dietary Fiber**    |       |       |        |             |
| Konjac glucomannan   |       |       | ↓      |             |
| Beta-glucan          | →     | ↓    | ↓      | →           |
| Increased dietary fiber intake | ↑ or → | ↓ | → | |
| Whole-grain foods    | →     | ↓    | ↓      | →           |
| Polyglycoplex        | →     | ↓    | ↓      | →           |
| Barley               | →     | ↓    | ↓      | →           |
| Psyllium             | ↓     | ↓    | ↓      | →           |
| **Soy and non-soy Legume consumption** |       |       |        |             |
| Soy                  | ↑     | ↓    | ↓      | ↓           |
| Soy products         | ↑     | ↓    | ↓      | ↓           |
| Soy protein          | ↑     | ↓    | ↓      | ↓           |
| **Fatty Acids**      |       |       |        |             |
| SFA                  | ↑     | ↑    | ↑      |             |
| Industrially produced-TFA | ↓  | ↑ |     |             |
| Ruminant-TFA         | →     | →    | →      |             |
| CLA                  | →     | ↓    | ↓      | →           |
| n-3 PUFA             | → or ↑| → or ↓| ↓      | WC ↓ or BMI → |
| MUFA                 | → or ↑| → or ↓| or ↑  | or ↓ or BMI → |

BMI: body mass index; BW: body weight; CLA: conjugated linoleic acid; GI: glycemic index; HDL-C: high-density lipoprotein-cholesterol; LC: low carbohydrate; LDL-C: low-density lipoprotein-cholesterol; LF: low fat; MUFA: mono-unsaturated fatty acid; PUFA: poly-unsaturated fatty acid; SFA: saturated fatty acid; TFA: trans fatty acid; TG: triglyceride; WC: waist circumference.
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