Committee Report 2

Diagnostic Criteria for Dyslipidemia

— Executive Summary of Japan Atherosclerosis Society (JAS) Guideline for Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases for Japanese

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Epidemiological studies have shown that the incidence of coronary artery disease increases as the LDL-C, TC, and TG levels rise and the HDL-C level lowers both in Japan and in Western countries (Fig. 1). At present, prevalence of coronary artery disease in Japan is much lower than that in Western countries. However, recent increases in the LDL-C and TC levels in Japanese associated with so-called Westernization of diet implies future increases in coronary artery disease. In this guideline, therefore, criteria for the diagnosis of dyslipidemia were defined as in Table 1, with a greater emphasis on the prevention of coronary artery disease.

The first step in this diagnostic procedure is to measure TC, TG, and HDL-C levels after overnight fasting. LDL-C level is then calculated by use of the Friedewald equation (LDL-C = TC - HDL-C - TG/5). The LDL-C level may be measured by a homogenous method especially in the case of postprandial examination or when the TG level is 400 mg/dL or higher.

1. High-LDL-Cholesterolemia

Results of many epidemiological studies conducted in Western countries, including the Framingham study, have shown that the morbidity and mortality of coronary artery disease increase with elevations in the TC level (LDL-C level). Also in Japan, the relative risk of coronary artery disease has been confirmed to increase continuously with rise in the LDL-C and TC levels by epidemiological studies such as NIPPON DATA 80, the Hiroshima/Nagasaki Study, Ministry of Health and Welfare Primary Hyperlipidemia Study, 3M Study, an epidemiological study at 76 workplaces, Okinawa Cohort Study, and Ehime Epidemiological Study.

In NIPPON DATA 80, a prospective epidemiological study in Japan, the relative risk of death due to coronary artery disease has been shown to increase 1.4, 1.7, 1.8, and 3.8 times when the TC level is 200-219, 220-239, 240-259, and 260 mg/dL or higher, respectively, compared with the group with a TC level of 160-179 mg/dL with males and females combined.

Since the relationship between TC and the morbidity and mortality of coronary artery disease is continuous over a broad range of TC levels without clear threshold, it is difficult to define a borderline for hypercholesterolemia.

On the other hand, it has been shown in Western countries that cholesterol lowering therapy including lifestyle improvement can significantly reduce the incidence of cardiovascular diseases. Also in Japan, results of large-scale clinical studies have recently been reported, demonstrating preventive effect of LDL-Lowering against atherosclerotic diseases.

On the basis of the relationship between the TC level and mortality due to coronary artery disease shown by the MRFIT, the NCEP, which is a guideline for lipid management in the United States, defines a TC level of 240 mg/dL, at which the relative risk of coronary artery disease doubles compared with that at 200 mg/dL, as a criterion of hypercholesterolemia.

In consideration of these evidences, we adopted a TC level of 220 mg/dL, at which the relative risk of coronary artery disease increases 1.5 times compared with that at 160-179 mg/dL according to NIPPON...
DATA 80, as a screening criterion for Japanese from a preventive viewpoint, and set an LDL-C level of 140 mg/dL, which corresponds to this TC level, as a criterion for high-LDL-cholesterolemia.

2. Low-HDL-Cholesterolemia

A significant negative correlation between the HDL-C level and the risk of coronary artery disease has been established not only in Western countries but also in Japan. However, there is no threshold HDL-C level for the relationship between HDL-C levels the morbidity of coronary artery disease is continuous over a broad range of LDL-C, and it is difficult to define a borderline for low-HDL-C, similarly to high-LDL-C. A Japanese epidemiological study reported that the risk of coronary artery disease increases rapidly as the HDL-C level decreases to the level less than 40 mg/dL. (Fig. 1b). The NCEP-ATPIII defines an HDL-C level below 40 mg/dL as low-HDL-C.

In consideration of these reports, the current guideline defines an HDL-C level below 40 mg/dL as low-HDL-C. While the HDL-C level is generally higher in females than in males, there is insufficient evidence concerning the relationship between the gender difference in HDL-C and the risk of coronary artery disease. Therefore, this guideline applies the single criterion to both males and females. Low-HDL-C is a risk factor of coronary artery disease, and the risk of coronary artery disease decreases as the HDL-C level increases.

3. Hypertriglyceridemia

Although there have been a number of reports on the positive correlation between the TG level and morbidity of coronary artery disease in Japan as well as in Western countries, the issue remains controversial. Particularly, disappearance of the association after correction for the HDL-C level has been reported in a number of studies. Recently, significant association between the TG level and coronary artery disease has been suggested by 2 Japanese cohort studies (Fig. 1c). A Japanese epidemiological study showed that the morbidity of coronary artery disease increases when the TG level is 150 mg/dL or higher.

Table 1. Diagnostic criteria for dyslipidemia (Serum sampled after overnight fasting)

<table>
<thead>
<tr>
<th>Lipid Type</th>
<th>Criterion</th>
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<tbody>
<tr>
<td>LDL-cholesterol</td>
<td>≥ 140 mg/dL</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>&lt; 40 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>≥ 150 mg/dL</td>
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Diagnosis of dyslipidemia is made when either type of lipid abnormalities is present. These diagnostic criteria are not intended for the beginning of drug therapy. It is important to consider the indications of drug therapy only after evaluation of other risk factors. LDL-C is evaluated basically by calculation with the Friedewald equation. 

\[
\text{LDL-C} = \text{TC} - \text{HDL-C} - \frac{\text{TG}}{5} \quad \text{(when TG is < 400 mg/dL)}
\]

When the TG is ≥ 400 mg/dL or non-fasting state, the LDL-C should be determined by direct measurement.
Also in the United States, a TG level of 150 mg/dL or higher is regarded as hypertriglyceridemia on the basis of the Framingham study. In consideration of these results, the current guideline defines a TG level of 150 mg/dL or above as hypertriglyceridemia. However, hypertriglyceridemia often has other important implications such as an increase in remnant lipoprotein, increase in small dense LDL, and complication of low-HDL-C. Therefore, possible association of these metabolic abnormalities should be kept in mind upon management of elevated TG level.

References
17) Tarui S: 1987 in Japanese
21) Chikamori T, Sugimoto K, Hamada T, Kitaoik H, Furuno T, Sato H, and Doi Y: Efficacy of cholesterol lowering treatment in Japanese elderly patients with coronary ar-