

## Problems that Physicians should Notice for Better Treatment of Hypercholesterolemia in Japan

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Regulation of serum lipid profiles, especially low-density lipoprotein-cholesterol (LDL-C) levels, is receiving remarkable attention from not only medical experts but also general public. Then, even after providing LDL-C lowering therapy, residual risk sometimes comes to an issue for further reduction of atherosclerotic cardiovascular diseases (ASCVD). However, the means to reduce LDL-C levels and the ideal target level of LDL-C are still the most important themes. To promote effective lipid management in Japan, Japanese Atherosclerosis Society (JAS) continuously recommends ways to treat dyslipidemia and proposes the specific target levels of LDL-C, which are also published in the newest guideline 2017<sup>1)</sup>. However, in the cohort of patients with high cardiovascular risk in 2013, Teramoto et al. reported that approximately 68% of the overall population achieved guideline that recommended levels of LDL-C with only 42% receiving current treatment with statins<sup>2)</sup>.

Recently, Yamashita *et al.* reported the current status of physician awareness and attitudes for lipid-lowering therapy<sup>3)</sup>. In January 2017, authors conducted web-based survey in 500 Japanese physicians, 100 in each of five categories: cardiology; diabetes, metabolism, and endocrinology; neurology/neurosurgery/stroke medicine; general internal medicine (hospitals  $\geq$  20 beds); and general internal medicine (self-employed practitioners at clinics or small hospitals  $\leq$  19 beds). This survey revealed three important problems. First, there exists a difference among physicians in their specialties about the target LDL-C level. Second, the general physicians in Japan may be treating undiagnosed familial hypercholesterolemia (FH) patients. Third, there is a low rate in the use of non-HDL-C level and the risk management chart.

At first, essentially, most physicians (over 95%) recognized high LDL-C level as an important risk for ASCVD. The mean target level for physicians with expertise in cardiology was the lowest of all the areas of clinical expertise ( $92.6 \pm 17.3$  mg/dL), and in patients with a history or complications of diabetes, chronic kidney disease, noncardiogenic cerebral infarction, or peripheral arterial disease, the overall target level was  $112.7 \pm 17.4$  mg/dL.

As for the statin therapy, participants were most concerned about muscle disorders as adverse effect, followed by new onset diabetes. In addition, physicians with expertise in neurology/neurosurgery/stroke were about twice as likely as other participants to agree with the statement "Japanese with low LDL-C are more likely to develop cerebral hemorrhage", while over 70% of participants expressed concern about safety at LDL-C below 70 mg/dL.

The authors stated that cardiology specialists tend to practice lipid-lowering treatment more aggressively than those with other areas of medical expertise, which may be because they generally treat secondary prevention patients and that the increasing number of patients who are candidates for secondary prevention of ASCVD could predispose these specialists to develop a mindset toward ASCVD therapy similar to that seen in the US and Europe. In addition, they suggested that less aggressive LDL-C target setting by the physicians with expertise in neurology/neurosurgery/stroke might be partially related to their sense that the Japanese patients are generally at low risk for CV events even without achieving the currently recommended lipid levels. These results and comments may faithfully reflect current opinion of Japanese physicians and suggest several issues to overcome against the low rate of treatment for hypercholesterolemia.

Next, 65.4% of participants had treated patients with FH, but the percentage was lower in physicians

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with clinical expertise in neurology/neurosurgery/stroke and general internal medicine than others. Only 45% of participants examined X-ray photographs of Achilles tendon. A research in Japan also stated that among the diagnosed and suspected FH patients, 83.5% had not achieved the LDL-C level of <100 mg/dL recommended for patients with FH at the index date, and 44.5% of the patients were not currently treated with lipid-modifying therapies<sup>4)</sup>. To improve the diagnostic capability of FH in physicians, it may be useful to adopt ultrasonography rather than X-ray photographs in addition to further information about FH characteristics<sup>5)</sup>.

Finally, 62% of participants stated that they did not use the “non-HDL-C” level. Furthermore, although 62.6% of participants knew about the risk management chart, only about 20% of them used the chart.

Thus, these problems may be caused by the fact that the understanding of the lipid metabolism, diagnosis, and therapy of dyslipidemia is still not widespread, although most physicians recognize high LDL cholesterol level as an important risk for ASCVD. It is possible to improve upon the three issues described above. However, there still exists a difficult problem. NIPPON DATA2010 Research Group revealed that hypercholesterolemia is associated with genetic background, lifestyle including diet pattern, and socioeconomic status including employment status, length of education, marital status, and household expenditures<sup>6,7)</sup>. They also demonstrated that among the participants with hypercholesterolemia, 55.4% of men and 55.1% of women were not receiving medication<sup>7)</sup>. Nevertheless, we hope that authors will plan to develop interactive educational programs focusing on the management of dyslipidemia and to offer these programs as training courses on a regular basis.

### Conflict of Interest

None.

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