Editorial

Participants with Treated Hyperlipidemia may be More Health Conscious

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Hyperlipidemia is a well-known risk factor of coronary heart diseases, and the beneficial effect of hyperlipidemia treatment on coronary disease prevention was well established¹⁻³. Actually, US preventive service task force strongly recommends the screening of high blood cholesterol and its early treatment⁴. However, to interpret the relationship of total cholesterol with all-cause mortality, several issues to be discussed were previously raised^{5,6}. A report by Daimon, *et al.* contains these issues⁷. In this editorial, we would like to introduce these topics.

Daimon *et al.* reported the relation of treated hyperlipidemia, untreated hyperlipidemia, and non-hyperlipidemia participants with total mortality⁷. They concluded that participants with untreated hyperlipidemia showed a higher risk of total mortality than those with treated hyperlipidemia.

Their observation that treated hyperlipidemia participants showed a lower risk than untreated hyperlipidemia participants was in line with previous RCTs¹⁻³. It is confirmative that participants with hypercholesterolemia can improve their prognosis using lipid lowering medications just as clearly indicated in clinical guidelines worldwide¹⁻³.

However, present finding was too striking, i.e., hazard ratio (95% confidence interval) of participants with treated hyperlipidemia was 0.24 (0.08–0.69) compared with those with untreated hyperlipidemia, which may mislead readers concerned about the real effects of medication for dyslipidemia. This specious large difference cannot be explained only by the effects

of lipid-lowering drugs; this difference can also be explained by the better health consciousness in treated hyperlipidemia participants.

Regarding hypertension, a previous study reported that only 24% of the untreated hypertensive participants who pointed out their high blood pressure at health check-up started treatment within 1 year⁸. Because Tanaka *et al.* reported that the percentage of untreated subjects with hypertension was significantly lower than the percentage of untreated subjects with hypercholesterolemia (41.0% vs. 57.1%, $p < 0.001$) in Japanese workers, the rate of starting lipid medication may be lower than that of starting antihypertensive medication⁹. These findings suggested that participants who treated hyperlipidemia were highly health conscious, which related to a healthy life style and good compliance for lifestyle modifications as advised by physicians. In the present study, Daimon *et al.* also revealed that the proportion of participants who were taking lipid lowering agents was only around 20% (313/1395) in all dyslipidemic participants. Higher health consciousness in participants with treated hyperlipidemia was also suggested by the prevalence of current smoker, which is an indicator of healthy lifestyle. Prevalence of current smoker was 9.3%, 20.5%, and 19.6% in participants with treated hyperlipidemia, untreated hyperlipidemia, and non-hyperlipidemia, respectively.

Thus, we could interpret the present findings that participants with treated hyperlipidemia showed a much lowest risk of total mortality not only because of the effect of lipid lowering medication but also because of higher health consciousness, in other words, a healthy lifestyle, their original personality, etc.

On the other hand, this paper revealed that crude mortality rate was lower in participants with hyperlipidemia without medication than in non-hyperlipidemic participants. Of course, this odd finding was diminished when they adjusted for possible confounders. However, the point estimate of risk was still lower in untreated hyperlipidemia than that in non-hyper-

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lipidemia participants. In previous studies, these findings that lower cholesterol was related to a higher mortality, particularly in non-coronary disease mortality, were observed. This finding may be mainly explained by subclinical exhausting condition, such as cancer, respiratory function, etc. For example, Okamura *et al.* investigated the relationship between total cholesterol and all-cause mortality¹⁰. In their report, the highest cholesterol category as well as the lowest cholesterol group showed a higher risk of all-cause mortality. This relationship was not found after excluding deaths in the first 5 years of follow-up, i.e., in the group with lower cholesterol, the proportion of exhausted condition, such as liver diseases, depression may be increased.

Another interpretation was unmeasured confounding. Serum cholesterol level was defined mainly by diet, particularly for saturated fat intake. This westernized dietary style may be the marker of participants' higher socio-economic status (SES), i.e., higher saturated fatty acid intake related to the high serum level of cholesterol may be associated with higher SES, particularly in the rural population. This may also partly explain the higher mortality in lower cholesterol groups. In any case, it is cautious to interpret the observational data. Careful discussion including biological mechanisms is required.

The study reported by Daimon *et al.*, raises several interesting points of discussion as shown above. The most important message may be that hypercholesterolemia participants with treatment show very low mortality. Together with the effect of lipid lowering agents, their better health consciousness may extend their life expectancies.

Conflicts of Interest

None.

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