Letter to the Editor

Smoking and oxidised high-density lipoprotein: a preliminary report

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Cigarette smoking is a risk factor for cardiovascular disease [1]. While various mechanisms are involved in this association, the reduction in the circulating level of high-density lipoprotein (HDL), a protective factor against cardiovascular disease, by smoking is well known [1]. Furthermore, smoking is a source of oxidants, leading to oxidative modification of *in vivo* molecules [1], and HDL is modified oxidatively as oxidised HDL (oxHDL) [2]. Because oxHDL lacks the native HDL function (i.e. suppression of the antioxidative function of apolipoprotein A-I, inhibition of ABCA1-dependent cholesterol efflux from atheromatous lesions) [1–3], the oxHDL behaviour may explain the association among smoking, HDL and cardiovascular disease.

At present, information concerning the relationship between oxHDL and smoking habits is limited. Although previous studies have not directly examined oxHDL itself, the antioxidant ability of HDL in smokers has been reported to be impaired [4, 5]. The blood level of oxidised lipids of HDL was reportedly low in young smokers (possibly due to the active removal of smoking-induced oxidants) [6]. Accordingly, the oxHDL levels in relation to smoking should be further examined.

The present study therefore investigated the oxHDL levels in smokers. A total of 90 asymptomatic subjects (smokers: n = 26) were enrolled in our study. Smoking habits were self-reported. We excluded subjects with a history of coronary diseases and the use of antioxidative, anti-hypertensive, anti-diabetic and lipid-lowering drugs. The Ethics Committee approved the study (No. 18-102, 19-rev17), and the subjects gave their informed consent. In fasted serum samples, lipid profiles were enzymatically measured, and oxHDL was measured using an enzyme-linked immunosorbent assay (Hoken-Kagaku West, Co. Ltd., Kyoto, Japan) [1]. A t-test and χ^2 test were performed for assessments between the groups, and a general linear analysis for oxHDL with adjustment for variables was also used. $P < 0.05$ was considered significant.

Table I shows the clinical characteristics of the subjects studied. Smokers had a lower level of total and HDL-cholesterol and a higher level of oxHDL and oxHDL/HDL-cholesterol than non-smokers. The difference in the oxHDL or oxHDL/HDL-cholesterol levels between smokers and non-smokers remained significant after adjusting for the age, gender and body mass index (oxHDL, $p = 0.01$; oxHDL/HDL-cholesterol, $p < 0.01$).

We thus detected high oxHDL levels in smokers. This finding is reasonable as smoking is assumed to oxidise lipoproteins, including HDL [4–6], and it is noteworthy to add the present finding to those of earlier

Table I. Clinical characteristics of studied subjects

Variables	Non-smokers (n = 64)	Smokers (n = 26)	P-value
Age [years]	55 ±15	56 ±12	0.79
Men, n (%)	35 (55)	13 (50)	0.69
Body mass index [kg/m^2]	24.2 ±3.7	24.5 ±4.4	0.77
Total cholesterol [mmol/l]	5.29 ±0.94	4.68 ±0.99	0.01
Triglyceride [mmol/l]	1.16 (0.80–1.57)	1.29 (0.88–2.01)	0.22
HDL-cholesterol [mmol/l]	1.51 ±0.44	1.23 ±0.44	< 0.01
OxHDL [ng/ml]	164 (111–252)	215 (176–513)	0.02
OxHDL/HDL-cholesterol	2.89 (1.88–4.81)	4.85 (2.80–14.3)	< 0.01

HDL – high-density lipoprotein, OxHDL – oxidised HDL. Characteristic data are shown as the mean ± standard deviation, median (interquartile range) or subject number (%). Triglyceride, oxHDL and oxHDL/HDL-cholesterol were calculated after log-transformation because of their skewed deviations. Significance (non-smokers versus smokers): p < 0.05.

studies, given the limited information available concerning the relationship between oxHDL and smoking [4–6].

However, the high oxHDL level in smokers appeared to conflict with the findings of an earlier study [6]. This discrepancy might be due in part to the difference in the population (younger people in the earlier study [6] than in the present study) and/or the methodology for measuring oxHDL markers. The measurements are of concern as various kinds of markers for HDL oxidation are currently being considered. Unlike the marker used in the earlier study [6], the oxHDL marker used in the present study reacts specifically with the oxidised apolipoprotein A-1, not native HDL [2]. Which markers are most suitable for assessing the relationship between HDL and smoking status should be explored in further studies. In addition, like the marker used in the present study, the easy measurement of oxHDL with a simple assay is also an important point that should be explored in further studies on this topic.

This study was a preliminary one with certain limitations. For example, the studied population was relatively small. In addition, the cross-sectional design did not discuss the causality. The smoking habit was self-reported, and the details concerning the smoking habit (e.g. pack-year, intensity) were not examined. These points will be addressed in future research.

In conclusion, the present study suggested that smokers have high levels of oxHDL. An oxHDL marker may be a potent target for evaluating the smoking-cardiovascular disease connection.

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Conflict of interest

The authors declare no conflict of interest.

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