Gender Difference in the Level of High-density Lipoprotein Cholesterol in Elderly Japanese Patients with Coronary Artery Disease

Haruki Musha, Akio Hayashi, Keisuke Kida, Eiji Takahashi, Kae Suzuki, Kensuke Kawasaki, Koji Inoue, Yoshihiro Akashi, Katsuhiko Tsuchiya, Masahiro Yamauchi, Tomoyuki Kunishima and Nobuyuki Hashimoto

Abstract

Objective High-density lipoprotein cholesterol (HDL-C) levels are known to be reduced in the metabolic syndrome, but the HDL-C profile of elderly patients with coronary artery disease (CAD) has not been well characterized. This study investigated the gender difference of HDL-C levels in elderly Japanese patients with CAD.

Methods Serum lipid data were analyzed retrospectively to assess sex-related differences of the lipid profile, and to evaluate the effects of pharmacotherapy or physical exercise on hyperlipidemia.

Patients A total of 163 elderly (≥65 years) outpatients with CAD (128 men aged 70.6±5.2 years and 35 women aged 74.1±6.0 years [mean±SD]) were investigated.

Results The mean total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels were similar in men and women, while the mean HDL-C level was significantly higher in women than men (58.3±18.1 vs. 50.3±13.5 mg/dL; p=0.0064). The HDL-C level was not significantly influenced by oral lipid-lowering therapy or regular exercise in either sex. However, women without lipid-lowering therapy had significantly higher HDL-C levels than men with (p=0.0312) or without (p=0.0338) lipid-lowering therapy, while women performing regular exercise had significantly higher HDL-C levels than men with (p=0.0047) or without (p<0.001) regular exercise.

Conclusion Elderly women with CAD have higher HDL-C levels relative to their postmenopausal state than those of men with CAD. Low HDL-C levels, unlike in men, may not be a major risk factor for CAD in elderly women.

Key words: elderly Japanese women, high-density lipoprotein cholesterol, coronary artery disease, gender difference

(International Medical Journal. 45.1528)
HDLC level in the increase of CAD in postmenopausal women (2), but few studies have addressed this issue in Japanese women. Accordingly, the purpose of this study was to investigate the gender difference of the HDLC profile in elderly Japanese patients with CAD, especially postmenopausal women.

Patients and Methods

The study involved 163 patients ≥65 years old who were treated at the outpatient department of Yokohama City Seibu Hospital for CAD, which was diagnosed by cardiac catheterization, radionuclide cardiac scintigraphy, and standard 12-lead electrocardiography. All of the patients gave written informed consent for the use of their clinical data in this study. The study was conducted after being approved by the ethical committee of St. Marianna University School of Medicine (approval number 613). The following blood lipid parameters were measured in the fasting state for each patient: total cholesterol (TC), low-density lipoprotein cholesterol (LDLC), HDLC, and triglycerides (TG). In some patients, HDLC subclasses (HDL2 and HDL3) were also measured after separation by dextran sulfate precipitation (3). The patients were asked about their exercise program by using a questionnaire. Those who had performed exercise for at least 30 minutes at least twice a week for a minimum of 1 year were defined as performing regular exercise. Results are expressed as the mean±standard deviation. Statistical analysis was performed using the \( \chi^2 \)-test or the unpaired \( t \)-test and differences were considered significant at \( p<0.05 \).

Results

Table 1 summarizes the clinical profile of the 163 patients. There were 35 women with a mean age of 74.1±6.0 years, which was similar to the mean age of the 128 men.
HDL subclasses (HDL₂ and HDL₃) (mean ± 1SD) in women and men. There were no significant differences between women and men for either HDL subclass.

Levels of HDL-C (mean ± 1SD) in women and men treated (+) or not treated (−) with a lipid-lowering agent. The HDL-C level of untreated women was significantly higher than that of either treated or untreated men.

The mean TC and LDL-C levels were similar for women and men (199.1±27.3 vs. 189.9±28.7 mg/dL and 106.7±19.3 vs. 110.8±22.8 mg/dL, respectively; Fig. 1). The mean HDL-C level was significantly higher in women than in men (58.3±18.1 vs. 50.3±13.5 mg/dL; p=0.0064), and the mean TG level was also higher in women than men (145.0±66.2 vs. 127.9±70.0 mg/dL, p=NS) (Fig. 2). HDL₃ and LDL₃ levels were also higher in women than in men, but these differences were not significant (26.4±9.8 vs. 22.9±8.0 mg/dL and 21.4±7.2 vs. 19.3±4.1 mg/dL, respectively; Fig. 3).

When analyzed with regard to oral lipid-lowering therapy, the HDL-C level was similar between treated and untreated women (56.8±18.3 vs. 62.2±17.9 mg/dL), as well as between treated and untreated men (50.2±12.4 vs. 50.4±14.8 mg/dL). However, the HDL-C level of untreated women was significantly higher than that of either treated or untreated men (Fig. 4). Although a low HDL-C (defined as <40 mg/dL) was found in statistically similar proportions of women (n=4; 11.4%) and men (n=25; 19.5%), all 4 women with low HDL-C levels were on lipid-lowering therapy versus 12 out of 25 men with low HDL-C levels.

Similar comparisons between patients with and without regular exercise showed higher HDL-C levels for the former among both women (63.3±18.7 vs. 51.1±16.9 mg/dL) and men (51.1±14.1 vs. 48.6±12.3 mg/dL), but there were no significant differences. However, the HDL-C level of women performing regular exercise was significantly higher than that of men with or without regular exercise (Fig. 5).
Discussion

Because of the established antiatherosclerotic effect of HDL-C (4-6), the level of this lipoprotein is thought to have considerable significance in the primary and secondary prevention of CAD, as indicated by inclusion of a low HDL-C level in the Japanese diagnostic criteria for metabolic syndrome (1). However, women have higher total cholesterol levels than men and often have high HDL-C levels, so the role of low HDL-C in the etiology of CAD among post-menopausal women is uncertain. In addition, the characteristic diet of elderly Japanese women includes carbohydrates as a greater proportion of the total energy intake compared with other age groups, which may increase the risk of high TG and low HDL-C levels in this population. The present study was performed to evaluate gender difference of HDL-C levels in elderly Japanese patients with CAD under routine treatment, as well as to evaluate the effects of pharmacotherapy and non-pharmacologic treatment (exercise) of hyperlipidemia on the HDL-C profile in elderly Japanese women.

Although the mean TC and LDL-C levels were similar, the HDL-C level of these elderly (i.e., postmenopausal) women was higher than that of the elderly men, indicating that a higher HDL-C level in women may not represent a direct effect of estrogen. A low HDL-C level (defined as <40 mg/dL by the Japanese diagnostic criteria for metabolic syndrome) was only found in women treated with cholesterol-lowering agents (e.g., statins). In contrast, it was seen in nearly 50% of men who were not on lipid-lowering medications. A low HDL-C level is an established risk factor for CAD in men (7). If a low HDL-C level in postmenopausal women with CAD is related to lipid-lowering therapy, it should be considered less significant as a risk factor or the current definition of low HDL-C for women should be revised. A low HDL-C level is defined as <50 mg/dL for women in the metabolic syndrome diagnostic criteria proposed by the Adult Treatment Panel III of the National Cholesterol Education Program (NCEP) (8). If a low HDL-C level is only defined as <50 mg/dL in women, as proposed by the NCEP, it would have been found in 8 female patients from our series (23%), i.e., a similar rate to that in our male patients. Therefore, the HDL-C threshold for women (40 mg/dL) in the current Japanese criteria, as well as the WHO definition (9), seems to be set too low for elderly Japanese women. There is a definite sex-related difference of HDL-C, even in the elderly, which should be taken into account when evaluating HDL-C data.

It has been reported that exercise increases the HDL-C level (10), but the present study failed to demonstrate a significant effect of exercise on the HDL-C level or HDL subclass levels in both women and men. Possible explanations for this failure include the lower baseline HDL-C level in these elderly CAD patients than in younger populations and the low level of physical activity (≥30 minutes) and low frequency (≥twice a week) used to define regular exercise. Additionally, the regular exercisers identified among elderly CAD patients in this study might have included many individuals who performed less intense activities such as walking, which might have reduced the total intensity of exercise. To clearly demonstrate any sex-related difference in the effect of exercise, a study should be designed to compare the lipid profile between patients performing or not performing more intense exercise or exercise for a longer duration and more frequently. Nevertheless, the present study showed that regular exercise tended to increase the HDL-C level, even in elderly patients with CAD and a mean age >70 years. This finding once again emphasizes the importance of regular exercise for the primary and secondary prevention of CAD by improving HDL-C regardless of age.

Limitations

This was a retrospective observational study performed in a small number of elderly patients who were being treated for CAD. To more fully define the effects of exercise and lipid-lowering therapy on the HDL-C level, it is necessary to perform a large-scale prospective randomized controlled study that compares non-pharmacologic and pharmacologic interventions.

This study was supported in part by grants from the Japan Heart Foundation.

References

3. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-Mg+ precipita-
tion procedure for quantitation of high-density lipoprotein cho-
4. Johansson J, Carlson LA, Landow U, Hamsten A. High density lipoproteins and coronary atherosclerosis. A strong inverse relation with the largest particles is confined to normotriglyceremic pa-
6. Okamura T, Hayakawa T, Kadowaki T, et al. The inverse relation-
ship between serum high-density lipoprotein cholesterol level and all-cause mortality in a 9.6-year follow-up study in the Japanese general population. Atherosclerosis 184: 143-150, 2006.


© 2006 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imindex.html