Committee Report 10

Women

Tamio Teramoto, Jun Sasaki, Hirotsugu Ueshima, Genshi Egusa, Makoto Kinoshita, Kazuaki Shimamoto, Hiroyuki Daida, Sadatoshi Biro, Kazuhiko Hirobe, Tohru Funahashi, Koutaro Yokote, and Masayuki Yokode

Committee for Epidemiology and Clinical Management of Atherosclerosis

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1. Age-Associated Changes in Serum Lipid Levels in Women

While the HDL-C level decreases after adolescence in men, it remains high in women, and continues to be higher than in men throughout all ages. In women, the LDL-C and TC levels generally begin to increase in the late 40s, surpass those in men during menopause, and remain higher than in men thereafter¹⁾.

2. Incidence of Coronary Artery Disease in Japanese Women

According to epidemiological studies in Okinawa and Shiga, the age-adjusted incidence of myocardial infarction in women aged 35–65 years is about 1/5–1/6 of that in men^{2,3)}. In women, the risk of coronary artery disease (CAD) increases after menopause, but it is still lower than in men. In an epidemiological survey at 76 workplaces throughout Japan (3M Study), also, the incidence of myocardial infarction in women in their 50s was about 1/5 that in men⁴⁾. The mortality statistics of the Ministry of Health, Labor, and Welfare, also, show that the mortality rate due to CAD in women is about 1/5 in the 50s, about 1/3 in the 60s, and about 1/2 even in the 70s compared with that in men⁵⁾. Changes in morbidity and mortality rates of CAD in women trail those in men with a delay of about 10 years^{6,7)}. However, aging of women is advancing, and elderly mortality due to myocardial infarction is increasing⁵⁾, so that measures in consideration of these changes will become important in the future.

3. Lifestyle and CAD in Women

According to a report of a 14-year follow-up of about 84,000 American women (aged 30–55 years at

registration), the incidence of CAD (non-fatal myocardial infarction + coronary deaths) was significantly lower at 0.43 in those with 3 good lifestyle factors, i.e., adequate exercise, no smoking, and proper diet, compared with the others⁸⁾. In Japan, there have been few large-scale studies on lifestyle and CAD in women, but JACSS, which is a multi-center joint study concerning acute coronary syndrome, showed that smoking was a very high-risk habit in women⁹⁾. JPHC Cohort 1, which is an epidemiological study concerning smoking and CAD in men and women aged 40–59 years, also confirmed that smoking significantly increases the risk of CAD in women, though not as markedly as in men, and that the risk decreases rapidly within 2 years after smoking cessation¹⁰⁾. In addition, NIPPON DATA80 also reported a significant 4-fold increase in stroke in women who were smoking 40 or more cigarettes per day compared with non-smokers¹¹⁾.

Concerning other aspects of lifestyle, i.e., exercise and diet, no one would argue that correction of insufficient exercise and inappropriate diet, which lead to the accumulation of visceral fat, is important also from the viewpoint of the prevention of metabolic syndrome.

4. Risk Factors and CAD in Women

In Japan, the TC level has been reported to associate with CAD in women, while the relationship was slightly weaker than in men¹²⁾. Japan Lipid Intervention Trial (J-LIT), in which 68% of the subjects were women, also showed that the relative risk of CAD increased with the LDL-C level after simvastatin treatment¹³⁾.

However, according to the results of JACSS, the TC level was not a significant risk factor in women, but hypercholesterolemia was a strong risk factor in men plus women aged less than 65 years⁹⁾. Further accumulation of data is required. High-HDL-choles-

terol, diabetes mellitus, and hypertension, which are coronary risk factors clarified in the Framingham study, are also important risk factors in women, indicated by studies in Japan including NIPPON DATA80 and JACSS^{9, 14}. Furthermore, TG has been reported to increase the risk of CAD in women¹⁵.

5. Primary and Secondary Prevention of CAD and Stroke in Women

In AFCAPS/TexCAPS, which was a large-scale clinical study evaluating primary prevention, the suppressive effect of a decrease in the lipid level by Lovastatin (not approved in Japan) treatment against CAD was shown to be greater in women than in men. However, the difference was not significant because of the small number of events¹⁶.

Concerning the studies in Japan, approximately 68% of the subjects in MEGA, a recent study in which the primary preventive effect of pravastatin was evaluated, were postmenopausal women aged 70 years or less. On sub-analysis concerning the women of MEGA, no significant difference was observed in the incidence of CAD between the pravastatin intervention group and dietary therapy alone group in women aged 55 years or above, with a hazard ratio of 0.65. However, in women aged 55 years and older, the hazard ratio of CAD + cerebral infarction was 0.63, and that of stroke was 0.47, indicating significant decreases in the incidences of these conditions in the pravastatin group¹⁷.

Concerning secondary prevention, sub-analysis of 4S indicated that the effectiveness of simvastatin in women was comparable to, or higher than, that in men with regard to the number of coronary artery events¹⁸, although the effect on the mortality was not conclusive because of the small number of deaths. Similarly, in CARE, a prevention study, a decrease in the lipid level brought about by pravastatin treatment was more effective in women than in men¹⁹. Although no significance was shown in each study, the relative risk of death due to CAD was reduced to 0.36 through the lipid lowering in women when the results of the 3 studies, Scottish Society of Physicians, Newcastle upon Tyne, 4S, are taken into account²⁰. Therefore appropriate treatment is considered to be necessary for secondary prevention in women as well as in men.

In Japan, there is little evidence supporting that dyslipidemia is a risk factor of CAD in premenopausal women. Not only the relative risk of CAD but also the absolute number of patients is considered to be very low in Japanese premenopausal women. In addition, previous reports in Japan characteristically included many premenopausal women who were suspected of

having CAD but exhibited no significant stenosis on coronary angiography and those with angitis and aortitis due to SLE unrelated to atherosclerotic lesions²¹.

According to the results of the Chicago Heart Association Detection Project in Industry, in which the long-term prognosis was evaluated, the risk of CAD was at the very low level as 0.27, and total mortality was significantly reduced, in middle-aged women (aged 40–59 years) with no risk factor (TC level <200 mg/dL, blood pressure <120/80 mmHg, currently not smoking) compared with those with these risk factors²². Also, according to the results of the above cohort study concerning lifestyle and the incidence of CAD in about 84,000 American women (aged 30–55 years at registration), the incidence of CAD was 50% or less in those with 3 good lifestyle factors, i.e., proper diet, adequate exercise, and no smoking, compared with the others⁸.

Presently, the incidence of CAD in Japanese women is considerably lower compared with those in Western populations. However, one should be cautious, since the Westernization of the diet, lack of exercise, and a rise in the rate of smoking among women are increasing. Moreover, in anticipation of the further aging of the Japanese population due to it having the world's longest life expectancy, efforts to reduce risk factors of atherosclerosis through guidance to improve lifestyle from young age are extremely important also in women.

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