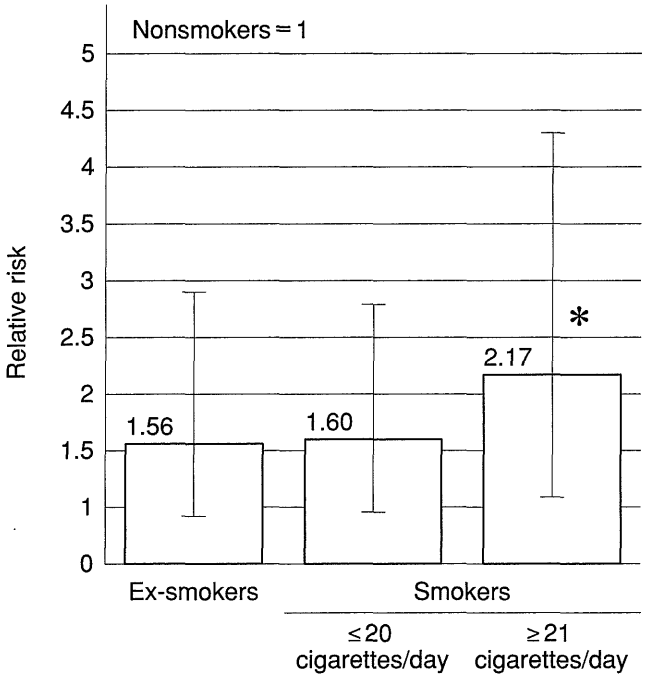

Fig. 1. Relative Risks (with 95% CI) of Death from Cerebrovascular Diseases Associated with Smoking, Follow-up of 51,774 man-years, the NIPPON DATA80.

The data were adjusted for age, systolic blood pressure, BMI, the TC level, alcohol intake and DM.
CI: Confidence interval
*: $p<0.05$ compared with nonsmoker group
Schematic diagram obtained from Ueshima H et al. Stroke. 35: 1836-1841, 2004

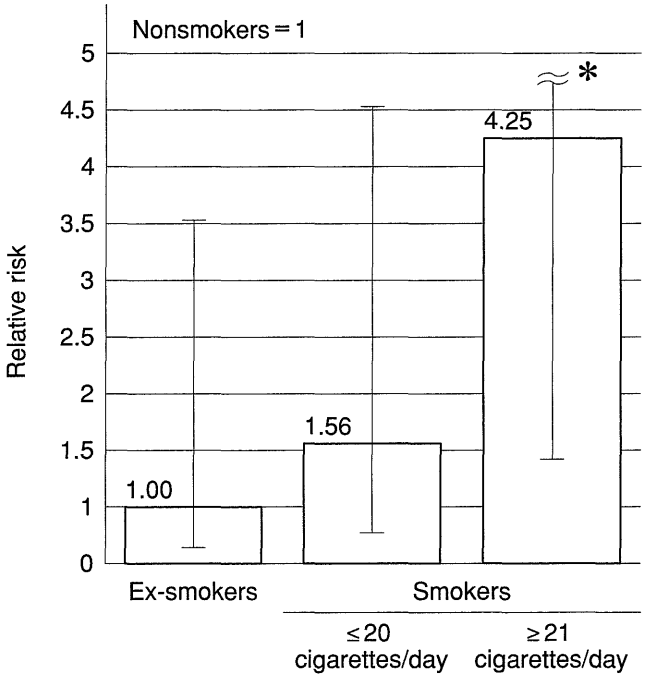

Fig. 2. Relative Risk (with 95% CI) of CAD-related Death Associated with Smoking, Follow-up of 51,774 man-years, the NIPPON DATA80.

The data were adjusted for age, systolic blood pressure, BMI, the TC level, alcohol intake and DM.
CI: Confidence interval
*: $p<0.05$ compared with nonsmoker group
Schematic diagram obtained from Ueshima H et al. Stroke. 35: 1836-1841, 2004

Table 1. Risk Factors or Markers to Consider

Lipid-related factors/markers	Non-lipid factors/markers
• Lp(a)	• C-reactive protein (CRP)
• Remnant lipoproteins	• Inflammation-related markers
• Small dense LDL	• Homocysteine
• Oxidized LDL and MDA-LDL	• Coagulation/fibrinolytic factors
• Apo B	
• Ratio of lipids or apoproteins	

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Committee Report 6

Other High-Risk Conditions

Executive Summary of the Japan Atherosclerosis Society (JAS) Guidelines for the Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases in Japan −2012 Version

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Committee for Epidemiology and Clinical Management of Atherosclerosis

1. History of Coronary Artery Disease (CAD)

Epidemiological studies and interventional trials conducted in Western countries and the results of a meta-analysis of these studies have revealed that the incidence of cardiovascular events in patients with a history of CAD is higher than that observed in primary prevention patients.

In Japan, the incidence of cardiovascular events in primary prevention subjects in the J-LIT trial was 0.9/1,000 person-years[1], while that in secondary prevention patients was higher, with a value of 4.5/1,000 person-years[2]. The JCAD[3] and CREDO-Kyoto[4], registration studies of patients with CAD, reported the incidence of cardiovascular events to be ≥ 15/1,000 person-years. Among secondary prevention patients, there are further high-risk conditions, including acute coronary syndrome, smoking, diabetes mellitus, metabolic syndrome, chronic kidney disease, noncardiogenic cerebral infarction, peripheral artery disease and a constellation of risk factors. It has been reported that these patients clearly have a high incidence of recurrent coronary events, even when the LDL cholesterol (LDL-C) level is managed to the same extent as that in patients without complications.

2. Cerebrovascular Disease

It is well known that patients with a history of cerebrovascular disease are at a high risk for CAD.

It has been reported that the annual incidence of myocardial infarction in stroke patients ranges from 0.40% to 0.45% (4.0 to 4.5 persons/1,000 person-years) in Japan[5, 6]. Based on these figures, the incidence of myocardial infarction over 10 years in stroke patients is approximately 3.9% to 4.4%, suggesting that Japanese stroke patients are also at a high risk of developing CAD. In particular, noncardiogenic cerebral infarctions are derived from atherosclerotic lesions and are therefore a high-risk condition for CAD.

3. Chronic Kidney Disease (CKD)

Chronic kidney disease (CKD) is defined as the presence of kidney damage and/or a decreased kidney function lasting for ≥3 months. The former is determined according to the levels of albuminuria/proteinuria, and the latter is evaluated based on a decreased glomerular filtration rate (GFR). In the Evidence-based Practice Guidelines for the Treatment of CKD 2009 issued by the Japanese Society of Nephrology, CKD is divided into stages 1 to 5, with a therapeutic plan proposed for each stage[7] (see footnote).

CKD is a high-risk condition for cardiovascular disease (CVD)[8]. Large-scale observational cohort studies conducted in the Japanese general population, including the NIPPON DATA80, Suita study and JALS-ECC trials[9-13], have demonstrated that CKD is associated with an approximately 2-fold higher risk of CVD. In a post hoc analysis of the CASE-J trial investigating the effects of antihypertensive agents on CVD in Japanese patients with hypertension[14], the relative risks associated with various risk factors were compared. The analysis showed that CKD exhibits a significant association with cardiovascular risks (relative risk: 2.8) that is comparable to or even stronger than that with a history of cerebrovascular disease (relative risk: 2.2), heart disease (relative risk: 2.2) or type 2 diabetes (relative risk: 2.0).

The exacerbation of classical risk factors associated with CKD, such as blood pressure, the lipid levels and glucose metabolism, contributes to the

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increased risk of CVD observed in patients with CKD[8]. Regarding lipids, CKD is a representative cause of secondary hyperlipidemia; nephrotic syndrome[15] is often accompanied by hyper-LDL cholesterolemia, while chronic renal failure[16] is often accompanied by hypertriglyceridemia due to the accumulation of remnant lipoproteins or a high VLDL level and hypo-HDL cholesterolemia. The non HDL cholesterol (HDL-C) level, the sum of the levels of cholesterol in TG-rich lipoproteins and LDL, has been reported to be an independent factor associated with the carotid artery intima-media thickness (IMT)[17] and pulse wave velocity (PWV)[18] in CKD patients. The ARIC[19], an epidemiological study conducted in the US general population, demonstrated that higher total cholesterol (TC) or triglycerides (TG) levels are associated with a higher risk of incident CAD, regardless of the GFR. In contrast, the HDL-C level is not associated with a risk of CAD in patients with a low GFR, suggesting that the non HDL-C level is related to the development of CAD in CKD patients with a low GFR. Therefore, dyslipidemia is closely associated with CVD in patients with CKD.

The risk of CVD is high in the presence of CKD. There is, however, controversy over whether CKD itself is the cause of CVD. It may be that there are common risk factors that adversely affect both CKD and CVD. Meanwhile, in a model adjusted for classical risk factors, the presence or absence of CKD was found to be independently associated with CVD, suggesting the involvement of non-classical risk factors associated with CKD[8]. In any case, CKD should be treated as a high-risk condition for CVD[20].

Footnote

CKD is currently classified based on the cause, GFR category and albuminuria (or proteinuria) category (CGA), as proposed by the 'KDIGO 2012 Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease' and the 'Clinical Practice Guidebook for the Diagnosis and Treatment of Chronic Kidney Disease 2012' issued by the Japanese Society of Nephrology.

4. Peripheral Arterial Disease (PAD) and Abdominal Aortic Aneurysm (AAA)

Peripheral arterial disease was traditionally called ASO (arteriosclerosis obliterans) in Japan; however, in these guidelines, the term PAD[21] is used and the disease is defined as the presence of stenotic/obstructive lesions caused by atherosclerosis of the arteries in the extremities. PAD is characterized by symptoms such as coldness of the lower extremities, intermittent claudication, ulcers and necrosis. Abdominal aortic aneurysm (AAA) is a condition involving plaque formation and ulceration in the luminal face, as well as external saccular aneurysm formation due to atherosclerosis of the abdominal aorta. These atherosclerotic diseases (including carotid artery stenosis and renal artery stenosis) require treatments such as revascularization; however, managing the causative risk factors is also important. It should also be noted that the primary cause of death in patients with these diseases is CAD or cerebrovascular disease. Although epidemiological studies conducted in Western countries revealed long ago that these diseases are high-risk conditions for CVD, this has only recently been reported in Japan.

The REACH registry, a prospective epidemiological study, reported that the incidence of CVD per year in 603 patients with coexisting PAD among 5,193 Japanese patients entered until 2004 was 1.25% for all deaths, 0.55% for cardiovascular death, 0.77% for nonfatal myocardial infarction, 1.56% for nonfatal stroke, 3.08% for cardiovascular death + nonfatal myocardial infarction + nonfatal stroke and 10.52% for cardiovascular death + nonfatal myocardial infarction + nonfatal stroke + hospitalization[5]. These values are comparable to those for patients with coexisting CAD. Furthermore, in a prospective observational study of 557 patients with PAD, Shigematsu *et al.* reported that the incidence of CVD over three years was 6.3% for cardiovascular death, 11.3% for heart disease, 7.0% for brain disease and 16.9% for lower extremity events[22].

Regarding AAA, Kioka *et al.* performed preoperative coronary angiography in 94 Japanese patients who underwent elective surgery for AAA (81 men; mean age: 71.7 ± 6.4 years) and reported that complications of CAD were observed in 45.7% of the patients[23]. Similarly, Takigawa *et al.* reported that the complication rate for asymptomatic CAD detected on coronary angiography in 201 Japanese patients who underwent elective surgery for AAA (161 men; mean: age 73.1 ± 7.7 years) was 29.4%[24]. Hirose *et al.* performed ATP-loading myocardial single-photon emission computed tomography (SPECT) in a total of 788 Japanese patients, including 500 patients with aortic aneurysms, 183 patients with lower extremity PAD and 105 patients with combined aortic aneurysms and lower extremity PAD, who had not been diagnosed with CAD and reported that myocardial ischemia was observed in 77% of the patients with combined aortic aneurysms and PAD, 55% of the patients with PAD and 37% of the patients with aortic aneurysms[25]. These reports demonstrate that the existence of PAD

and AAA is also an important high-risk condition for CVD in Japanese patients.

Atherosclerotic findings in the carotid artery are independent risk factors for CVD[26, 27]. Thickening of the common carotid artery IMT on ultrasonography is associated with an increased incidence of CVD. In addition, the existence of plaque and its characteristics (e.g., low-intensity features and the formation of ulcers) is involved in the development of CVD[28, 29]. In Japan, it has been reported that IMT is an independent significant predictive factor for CAD as well as cerebral infarction[30-32]. In several reports, the extent of IMT has been found to be significantly correlated with the extent of coronary atherosclerosis[33, 34]. Shimada *et al.* reported that 37% of patients with carotid artery stenosis who underwent carotid endarterectomy presented with coronary lesions on preoperative coronary angiography, half of whom presented with triple-vessel disease or left main CAD[35].

Atherosclerotic renal artery stenosis is a cause of renovascular hypertension. It has been reported that 5% to 22% of elderly patients with CKD have coexisting renal artery stenosis. Renal artery stenosis is also a risk factor for CVD, and the complication rate for atherosclerotic disease in other organs is high[7, 36-38]. In the primary prevention of CVD, carotid artery findings and renal artery stenosis should be noted.

As noted above, it has been reported that AAA, carotid artery lesions and renal artery stenosis are associated with CVD; however, it is difficult to say that sufficient results of prospective studies in Japan have been accumulated. Therefore, these guidelines include only PAD as a high-risk condition.

Footnotes

This is an English version of the guidelines of the Japan Atherosclerosis Society (Chapter 6) published in Japanese in June 2012.

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Committee Report 7-A

Treatment A) Lifestyle Modification

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Committee for Epidemiology and Clinical Management of Atherosclerosis

1. Overview of Lifestyle Modification

Cardiovascular disease (CVD) develops by various environmental factors such as overeating and low physical activity on the top of genetic predispositions. Many epidemiological studies have revealed that the excessive intake of cholesterol and animal fat (saturated fatty acids) results in increased serum total cholesterol (TC) levels. Overeating and low physical activity are primary causes of metabolic syndrome that lead to abdominal obesity, glucose intolerance, increased blood pressure and triglyceride (TG) levels and decreased HDL-C levels. Such imbalances in lifestyle result in CVDs, such as myocardial infarction. According to the Hisayama study, the prevalence of obesity, impaired glucose tolerance and hypercholesterolemia was increased over 1961, 1974 and 1988 in both men and women, while that of hypertension and smoking decreased, as risk factors for cerebrovascular disease[1]. The National Nutrition Survey in Japan showed marked decrease in consumption of rice and all types of grains from 1946 to 1990 while that of milk, dairy products and meat markedly increased, indicating the Westernization of Japanese dietary habits[2]. Therefore, prevention of CVD should be based in principle on stop smoking, maintaining ideal body weight, restriction of animal fat and cholesterol intake, reduction of salt intake, and increase of fish, vegetables and fruits, and perform aerobic exercise for at least 30 minutes per day (**Table 1**).

Table 1. Lifestyle Modification for the Prevention of CVD

1. Stop smoking and avoid passive smoking.
2. Refrain from overeating and maintain an ideal body weight.
3. Reduce intake of meat fat, dairy products and egg yolk and increase the intake of fish and soy products.
4. Increase intake of vegetables, fruit, unrefined grains and seaweed.
5. Reduce intake of food containing too much salt.
6. Avoid excessive alcohol consumption.
7. Perform aerobic exercise for at least 30 min daily.

2. Smoking Cessation

Smoking is an independent risk factor for CVD. It significantly increases the risk of cardiovascular death and death from any cause[3, 4], and cessation of smoking reduces a risk of death and incidence of CVD regardless a past history of coronary artery disease (CAD), age and sex[4-9]. The effects of smoking cessation are immediate and a longer cessation period is associated with a further decrease in risk[5]. Therefore, people of all ages should be advised to stop smoking to prevent CVD. However, providing smoking cessation instructions in an outpatient setting is not always easy, and long-term counseling based on relevant procedures is often needed[10]. Because the rate of smoking cessation significantly increases 1.3-fold when a clinician spends only a few minutes to advise a patient to stop smoking[10], the Guidelines for Smoking Cessation issued by nine societies, including the Japanese Circulation Society, recommend the use of an instructional method known as the "5A approach" (Ask, Advise, Assess, Assist, Arrange), which can be performed in the short term in routine outpatient or screening settings[11]. The details of this instructional procedure are presented in **Supplemental Table 1**. Smoking habits are associated with nicotine dependence to varying degrees. A meta-analysis demonstrated that, as a treatment for nicotine dependence,

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nicotine replacement therapy with a nicotine patch or nicotine gum, or the use of varenicline, a $\alpha 4\beta 2$ nicotine receptor partial agonist, significantly increases the success rate of smoking cessation[12, 13]. Patient management for smoking cessation is covered by health insurance in Japan if certain requirements are met[14].

Meta-analyses conducted in overseas reported that passive smoking increases the relative risk of developing CAD 1.3-fold (95% CI: 1.2 to 1.4)[15], and that smoking bans in public places decrease the incidence of hospitalization due to acute coronary syndrome[16, 17]. Furthermore, a prospective study conducted in Japan showed that the hazard ratio for diabetes mellitus associated with passive smoking is 1.8 (95% CI: 1.1 to 3.1)[18]. Therefore, it is also important to instruct people to avoid passive smoking to prevent CVD.

3. Management of Obesity

To achieve and maintain an ideal body weight is an important target for lifestyle modification. Obesity, especially excess visceral fat accumulation, is considered to be an independent risk factor for CVD and promotes atherosclerosis directly or indirectly via dyslipidemia, impaired glucose tolerance, hypertension and dysregulated adipocytokine activity[19-22]. Therefore, it is important to achieve lifestyle modification through dietary management and exercise.

The status of body weight is evaluated based on the body mass index (BMI).

$$\text{BMI} = \text{body weight (kg)}/[\text{height (m)}]^2$$

In Japan, a BMI of 22 is considered to be an ideal body weight and a BMI of ≥25 is considered to be overweight[23]. A diagnosis of obesity as a disease is made when the obese people are currently or potentially accompanied by health problems[23]. Attention should be paid to visceral fat accumulation even if the BMI is within the normal range. For screening of obesity in daily clinical practice, a waist circumference at the umbilical level of ≥85 cm for men and ≥90 cm for women is used as the screening criteria for visceral fat accumulation[23, 24]. The area of visceral fat at the umbilical level can be measured more accurately using abdominal CT, in which an adipose tissue area of ≥100 cm^2 is defined as visceral obesity. Visceral fat accumulation is a central factor in the development of metabolic syndrome. Decreasing the amount of visceral fat can improve not only dyslipidemia, but also hypertension and impaired glucose tolerance[25].

The target of the body weight in treatment of obese patients should not immediately be set as a BMI of <25. It should be noted that acute weight loss in a short term by an aggressive approach such as a very low calorie diet may lead to rebound weight gain at a high rate. Weight loss through diet/exercise therapy is expected to provide relatively mild improvement in abnormalities in plasma lipids, blood glucose and blood pressure caused by obesity, even if the BMI is within the range of obesity. Therefore, it is advised to achieve a 5% decrease in body weight or waist circumference over three to six months and to maintain this achievement over time (**Supplemental Table 2**)[26, 27].

4. Diet Therapy

1) Diet and Dietary Habits for the Prevention of CVD

• Traditional Japanese Diet

The mortality from CAD in Japan is much lower than that observed in other developed countries due to several factors, including the effects of diet. Many epidemiological studies have shown that a traditional Japanese diet incorporating Japanese foods is effective for preventing CAD[28-39]. In the traditional Japanese diet, saturated fatty acids are supplied from meat and poultry, monounsaturated fatty acids are from meat, poultry, fish and vegetable oils, n-6 polyunsaturated fatty acids are from vegetable oils and soy products and n-3 polyunsaturated fatty acids are from seafood and plant foods. Cholesterol is derived from meat, eggs, fish and seafood[40]. More fish, soy and soy products are consumed than meat and eggs, and fatty acids are consumed in a balanced manner suitable for preventing atherosclerosis[40]. In addition, the consumption of millet and barley, low-polished rice, fruits, vegetables, seaweed and green tea contributes to a sufficient intake of dietary fiber, vitamins and minerals[41]. However, the Japanese diet has the disadvantage for health with a greater intake of salt; thus, it is necessary to make efforts to reduce the amount of salt intake. It has also been reported that maintaining the Japanese dietary pattern but with a lower salt content reduces mortality from CAD by approximately 20% as compared with a Western dietary pattern[42].

2) Optimization of Total Energy Intake and Energy Nutrient Ratio

• Maintenance of an Ideal Body Weight and Balance of Energy Nutrients

With diet therapy, appropriate energy intake to meet the demands of physical activity, aimed at maintaining an ideal body weight and balanced nutrient intakes, is the most important component of preventing CVD. The recommended percentage of energy derived from fat is 20% to 25%, while that from carbohydrates is 50% to 60%.

• **Lipids (Saturated/Unsaturated Fatty Acids and Cholesterol)**

It is essential to reduce the intake of saturated fatty acids and cholesterol, which are contained in large amounts in animal fat; however, there are significant individual differences in the absorption rate of cholesterol. Increased intake of saturated fatty acids has been reported to exacerbate insulin resistance and increase the LDL-C levels in Japan as well as in Western countries[43, 44]. In contrast, it has been reported in Japan that an extremely low intake of saturated fatty acids is associated with an increased incidence of cerebral hemorrhage[45, 46]; thus, the percentage of energy derived from saturated fatty acids should be at least 4.5% but less than 7%[47]. Meanwhile, excessive intake of trans unsaturated fatty acids, produced by the hydrogenation of polyunsaturated fatty acids which are contained in hard margarine and shortening, increases oxidized LDL, decreases HDL-C, and thereby increases the risk of CAD[48]. In order to reduce the intake of saturated fatty acids and cholesterol, meat with less fat should be selected and excessive intake of meat, dairy products and eggs should be avoided.

While the intake of saturated fatty acids should be reduced, the intake of unsaturated fatty acids should be increased. Patients should be instructed to consume more fish, especially bluefish, which is rich in n-3 polyunsaturated fatty acids. Epidemiological studies conducted in Japan have revealed a negative correlation between the intake of fish and n-3 polyunsaturated fatty acids and mortality from coronary events and myocardial infarction[49, 50]. These effects are considered to be mediated by TG-lowering effects, hypotensive effects, platelet aggregation inhibitory effects and improvements in the endothelial function achieved by n-3 polyunsaturated fatty acids, which are contained in large amounts in fish oil[51-54]. On the other hand, polyunsaturated fatty acids are easily oxidized; therefore, it should be noted that excessive intake of these fatty acids results in increased levels of oxidized LDL and decreased levels of HDL-C.

• **Selection of Carbohydrates**

Carbohydrates include sugar, which is digestible and absorbable, and dietary fiber, which is indigestible. The type and intake of carbohydrates affect glucose metabolism and the levels of TG and HDL-C. The glycemic index (GI) and glycemic load (GL) are indexes used to evaluate postprandial blood glucose following the intake of carbohydrates. Many studies have reported that these indexes exhibit positive correlations with the obesity index and the levels of TG and fasting blood glucose and a negative correlation with the level of HDL-C[55, 56].

An increased intake of dietary fiber inhibits fat absorption in the intestines and decreases the GI and GL. The intake of dietary fiber, especially soluble dietary fiber, has a LDL-C-lowering effect[56-59]. A relationship between the consumption of greater amounts of dietary fiber and decreased mortality from CAD and CVD has been reported[60, 61]. To ensure sufficient dietary fiber intake, consuming adequate amounts of plant foods, such as unrefined grains (e.g., brown rice, barley), soy (e.g., tofu, bean curd: natto, fermented soybeans), vegetables, seaweed, fruits and potatoes is useful. This leads to a low GI/GL diet.

• **Soy, Soy Products, Vegetables and Fruits**

It has been reported that the intake of plant foods from soy and soy products and their major components, isoflavones, is associated with inhibition of the development of CAD and cerebral infarction in women[62]. This is thought to be due to the mild decreases in the level of LDL-C, antioxidant effects, hypotensive effects and estrogen effects induced by the isoflavones[63-68], protein[69, 70] and polyunsaturated fatty acids contained in soy. The consumption of plant foods other than soy, such as fruits, vegetables[29, 71], pulses[71] and grains[72], as well as green tea, coffee and oolong tea, is also associated with inhibition of the development of CAD. In particular, a relationship between an increased intake of green tea and decreased mortality from CAD has been reported in Japanese women[73]. Plant sterols, rich in soy and germ, are expected to inhibit the absorption of exogenous cholesterol in the gastrointestinal tract[74-77]. A meta-analysis showed that an intake of plant sterols of ≥ 2 g/day results in decreases in the LDL-C level of up to 9%[78].

Frequent consumption of fruit and vegetables is recommended because these foods are low in calories and rich in dietary fiber, vitamins and minerals. It has also been reported that the intake of potassium[79], vitamin C[80] and vitamin B_6[81, 82] is associated with inhibition of the development of CAD.

• **Salt and Alcohol**

An excessive intake of salt increases blood pressure and promotes atherosclerosis. The intake of salt should be reduced to <6 g/day. Light to moderate alcohol consumption has been shown to be associated with the prevention of CAD[83], while excessive consumption of alcohol increases blood pressure and enhances TG synthesis in the liver.

3) Diet to Improve Risk Factors

Diet modification is essential for preventing CVD

Table 2. Nutrient Recommendations for the Prevention of Cardiovascular Disease

1. Maintain an ideal body weight (height [m]^2 × 22) in consideration of energy intake and the amount of physical activity.
2. Limit the energy percent derived from fat to 20%-25%, saturated fatty acids to ≥4.5% but <7%, and cholesterol intake to <200 mg/day.
3. Increase the intake of n-3 polyunsaturated fatty acids.
4. Limit the energy percent derived from carbohydrates to 50%-60%, and increase the dietary fiber intake.
5. Aim to reduce the salt intake to <6 g/day.
6. Limit alcohol consumption to ≤25 g/day.

because it is effective for managing the risk factors of CVD, as has been demonstrated in many studies. Patients should be given individualized dietary instructions in consideration of prior assessments of their lifestyles including their nutrient intakes (**Table 2**).

• **Hyper-LDL Cholesterolemia and Diet**

The intake of saturated fatty acids, cholesterol and trans unsaturated fatty acids, which increase the level of LDL-C, should be reduced. The percent energy from saturated fatty acids should be less than 7%, while cholesterol intake should be less than 200 mg/day. Specifically, the intake of meat, milk and eggs, which contain high amount of fat, should be limited. Furthermore, the intake of foods with LDL-C-lowering effects, particularly soluble dietary fiber and plant sterols, should be increased[84-86].

• **Hypertriglyceridemia and Diet**

The percentage of energy derived from carbohydrates should be slightly reduced, and excessive consumption of alcohol should be limited. The intake of n-3 polyunsaturated fatty acids should be increased. In patients with hyperchylomicronemia, fats should be limited more strictly. The percentage of energy derived from fat should be limited to less than 15%, comprised primarily of medium-chain fatty acids[87] or n-3 polyunsaturated fatty acids.

• **Hypo-HDL Cholesterolemia and Diet**

If the patient consumes alcohol moderately and exhibits no abnormalities in TGs, alcohol consumption does not need to be limited. Excessive intake of trans unsaturated fatty acids and n-6 polyunsaturated fatty acids should be limited.

• **Metabolic Syndrome and Diet**

In general, for patients with visceral fat accumulation and high insulin resistance, the total energy intake should be limited and a diet with a low percentage of energy derived from carbohydrates should be consumed. When selecting carbohydrates, low-GI/GL diets are desirable. Total caloric reduction with a moderate amount of fat in combination with exercise can improve insulin resistance and the components of metabolic syndrome, even if weight loss is modest.

• **Hypertension and Diet**

Efforts should be made to reduce the salt intake while increasing the fruit and vegetable intake. This leads to sodium restriction and sufficient intake of potassium, resulting in the promotion of urinary excretion of sodium. Excessive consumption of alcohol should be avoided because it increases blood pressure.

• **Diabetes Mellitus and Diet**

In patients with type 2 diabetes, amelioration of obesity is the most important component of disease management. Overeating should be avoided and the energy intake should be tailored for the level of daily physical activity. Hyperglycemia should be corrected by dividing the energy intake equally into the three meals, i.e. breakfast, lunch and dinner, whenever possible. Regarding the levels of energy intakes of nutrients, the ratio of sugar to other nutrients should not be increased. In particular, the intake of sugar and saturated fatty acids should be limited. In patients with type 1 diabetes, appropriate quantities of dietary energy should be consumed to maintain an ideal body weight, with consumption of a nutrient-balanced diet.

Glossary

Glycemic Index (GI) and Glycemic Load (GL)

The GI is a ranking of carbohydrates based on how much they raise blood glucose levels after the consumption of foods containing 50 g of carbohydrate. It is a relative index with 50 g of glucose serving as the reference value of 100. The GL is the value calculated from GI and is the amount of carbohydrate by which postprandial blood glucose change is predicted.

5. Exercise Therapy

Physical inactivity is associated with increased body fat (obesity), dyslipidemia, metabolic syndrome, hypertension, diabetes mellitus/impaired glucose toler-

Table 3. Guidelines for Exercise Therapy

Exercise intensity*	About 50% of maximum oxygen uptake
Intensity and frequency	At least 30 min per day (daily if possible) and at least 180 min per week
Type	Brisk walking, slow jogging, social dancing, swimming, cycling, bench step exercise, etc.

*Exercise intensity
(1) Estimated from the pulse rate during exercise (when exercise intensity is 50%) Heart rate (pulse rate/min) = 138 − (age/2)
(2) Estimated from perceived exertion:
11-13 on the Borg's scale (perceived exercise intensity)
(Fairly light to somewhat hard)
Maximum oxygen uptake: Index of whole-body endurance (cardio-respiratory endurance)

Borg's scale

Scale	Perceived
20	
19	Very, very hard
18	
17	Very hard
16	
15	Hard
14	
13	Somewhat hard
12	
11	Fairly light
10	
9	Very light
8	
7	Very, very light
6	

(Borg GA: Med Sci Sports Exerc. 1973; 5: 90-93.)

ance, vascular endothelial dysfunction, decreased exercise capacity and an increased risk of atherosclerotic CVD, such as CAD and cerebrovascular disease[88-98].

Increased physical activity maintains and increases exercise capacity, improves the serum lipid profile, decreases blood pressure, increases insulin sensitivity and glucose tolerance, improves the vascular endothelial function and prevents thrombosis[99-101]. In addition, it decreases mental stress and preserves the cognitive function[102, 103]. The amount of daily physical activity and leisure time physical activity and the level of physical fitness have been shown to be negatively correlated with mortality resulting from CVD and cancer as well as all-cause mortality[104-114]. Similar results have been observed in cohort studies conducted in Japan[88].

Exercise therapy includes aerobic endurance exercise and muscle resistance exercise. Aerobic exercise is effective in improving lipid metabolism[115-118]. The most commonly observed change in the serum lipid levels induced by exercise is an increase in the level of HDL-C. A meta-analysis of 25 randomized controlled trials (RCTs) that compared the effects of exercise therapy comprising ≥ 15 minutes of aerobic therapy for eight weeks with those of non-exercise therapy showed that the exercise therapy significantly increased the levels of HDL-C (Δ2.53 mg/dL, 95% CI: 1.36 to 3.70)[119]. The increased HDL-C levels exhibited a positive correlation with the length of exercise, and exercise of ≥ 121 minutes/week significantly increased the HDL-C levels. A meta-analysis of four RCTs conducted in Japan comparing the effects of aerobic exercise of mild to moderate intensity for 10 weeks to 24 months with those of non-exercise therapy showed that the exercise significantly increased the levels of HDL-C (Δ10.0 mg/dL, 95%CI: 5.39 to 14.65)[88].

Table 3 shows the basic guidelines for exercise therapy. Efforts should be made to increase physical activity in daily living and undertake exercise suited to the lifestyle of the individual. Aerobic exercise should be primarily performed, and brisk walking and slow jogging are recommended. Regarding the intensity of exercise, approximately 50% of the maximum oxygen uptake is suitable in terms of efficacy and safety. At 50% intensity, the increase in blood pressure observed during exercise is mild, blood lactate is not accumulated and exercise can be performed for an extended period of time. Exercise of at least 30 minutes duration per day at least three times per week (daily if possible) or of at least 180 minutes per week is desirable. For the elderly with a reduced muscle mass, aerobic exercise in combination with mild resistance (muscle) exercise is useful, and bench-stepping training, which can be performed in a room, is recommended[88]. The Ministry of Health, Labour and Welfare established the "Exercise and Physical Activity Guide for Health Promotion 2006" to prevent lifestyle-related diseases (**Supplemental Tables 3A to 3C**)[120]. A unit to express the quantity of exercise, the "Ekusasaizu (Ex) (= METs·hour)," was established, and the target quantity of physical activity to prevent lifestyle-related diseases was set at 23 Ex or more per week. For example,

walking or bicycling for 15 minutes, jogging or aerobics for 10 minutes and swimming for seven to eight minutes are equivalent to 1 Ex.

On the other hand, unaccustomed exercise carries a risk of musculoskeletal injury. For patients with CVD, strenuous exercise may cause sudden death or myocardial infarction[121, 122]. This requires careful consideration, and when exercise therapy is performed, complications of potential CVD and bone and joint disease should be assessed.

Footnotes

This is an English version of the guidelines of the Japan Atherosclerosis Society (Chapter 7-A) published in Japanese in June 2012.

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