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A Lipid-Lowering Diet Combined with Exercise is Effective for Achieving Healthy Serum Cholesterol in a Male with a Predisposition for Developing Hyperlipidemia (Dyslipidemia): A 20-Year Case Study

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Abstract: This case-study presents data supporting the use of a combination of a lipid-lowering diet and physical aerobic exercise for achieving healthy levels of plasma triglycerides, serum total cholesterol as well as low-density and high-density lipoproteins. The blood lipid data were those of one of the authors (Y.S.) obtained from annual health testing results from 1988 to 2011. Y.S. was diagnosed with hyperlipidemia (dyslipidemia) in 1989 and decided to not take lipid-lowering drugs but rather follow a lipid-lowering diet developed by a clinical registered dietician. The test results showed that initially, the lipid-lowering diet assisted in the achievement of healthy plasma triglyceride and total cholesterol levels. However, eight years after commencement of the lipid-lowering diet (in 1997) Y.S. had his second diagnosis of hyperlipidemia. He then included a daily walking program (no less than 10,000 steps per day, 5 to 6 days/week) and later indoor bike-peddling exercise (minimum of 30 min/day, 5 days/week) as part of his treatment plan and continued with his lipid-lowering diet. This new regimen was highly effective with Y.S. achieving and maintaining a healthy level of plasma triglyceride, serum total cholesterol as well as low-density lipoprotein cholesterol.

Keywords: hyperlipidemia (dyslipidemia); lipid-lowering diet; physical aerobic exercise; lifestyle modifications; a long case study

Introduction

Coronary artery disease (CAD) is the primary clinical manifestation of atherosclerosis and is the major cause of death in modern, industrialized countries as well as developing countries. Atherosclerosis also affects peripheral and cerebral arteries resulting in debilitating or life-threatening conditions [1]. Research has demonstrated a correlation between raised serum lipid levels, in particular cholesterol, and the incidence of coronary heart disease and atherosclerosis [2-7]. The Framingham Heart Study provided early epidemiologic evidence that low levels of serum cholesterol were associated with low rates of CAD, while high levels of serum cholesterol were associated with high rates of CAD [8].

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Cholesterol is constantly being used and synthesized. Humans synthesize 1.5-2 g/day of cholesterol (endogenous cholesterol), whereas about 0.3 g/day is provided by the average diet (exogenous cholesterol) [9]. The liver is the primary site of cholesterol synthesis, contributing about 1-1.5 g/day of the total quantity synthesized. Hepatic cholesterol is synthesized from acetyl-coenzyme A (acetyl-CoA) through a series of enzyme reactions. When dietary cholesterol intake is high, cholesterol feeds back to inhibit its own synthesis by inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme that converts HMG-CoA to mevalonic acid. Statins were developed to reduce cholesterol levels based on this feedback mechanism. They are now considered the first-line treatment for hyperlipidemia (dyslipidemia), because they competitively inhibit HMG-CoA reductase [10-13]. In fact, a series of large randomized trials have established the benefits of statins for lowering serum cholesterol level and the prevention of major fatal and non-fatal cardiovascular events [14-20]. The pharmacological management of blood lipids has thus proven beneficial for the prevention of CAD. However, statins are costly and have side effects as well as requiring medical supervision [21].

Research has also examined the efficacy of reducing lifestyle-related CAD risk factors for preventing the development of CAD [21-27]. Stampfer *et al.* [21] followed 84,129 female nurses, 30 to 55 years of age, participating in the Nurses' Health Study. These nurses did not have cardiovascular disease, cancer, or diabetes at baseline. The nurses were divided into either a "low-risk" or high risk category: Individuals were considered low-risk if they met the following criteria: 1) not currently smoking; 2) a body mass index (BMI) under 25 kg/m2; 3) consumed an average of half a glass of an alcoholic beverage per day; 4) engaged in moderate-to-vigorous physical activity (which could include brisk walking) for at least half an hour per day; and 5) scored in the highest 40 % of the cohort for consumption of a diet high in cereal fiber, marine n-3 fatty acids, and folate, with a high ratio of polyunsaturated to saturated fat, and low in trans-fat and glycemic load. A 14-year follow-up documented 1,128 major coronary events (296 deaths from CAD and 832 nonfatal infarctions), and demonstrated that the participants in the "low-risk" group (3 % of the population) showed an 83 % reduction in the incidence of CAD compared with the "high-risk" group (97 % of the population). Based on these results Stampfer et al. [21] concluded that "adopting a more healthful lifestyle (if people do not smoke cigarettes, are not overweight, maintain a healthful diet, exercise moderately or vigorously for half an hour a day, and consume alcohol moderately) could prevent a substantial majority of coronary disease events."

This case-study investigated whether a lifestyle-related program was effective in reducing risk factors associated with CAD. Specifically, the effect of a lipid-lowering diet and physical aerobic exercise on blood lipids was examined in a male who was diagnosed twice with hyperlipidemia between 1988 and 2011.

Methods

In annual health checkup, blood samples were drawn in the morning after a 12–14-hour fast.

(1) Case-study

Blood lipid data from one of the authors (Y.S.) obtained from annual health testing results from 1988 to 2011 were analyzed by the other two authors (N.S. and Y.N.) who are certified registered dieticians. The 1990, 1995 and 1998 blood test data were missing, as Y.S. did not attend the health check-up during those years.

The purpose of the analysis was to determine the use of a combination of a lipid-lowering diet and endurance exercise for achieving healthy levels of plasma triglycerides, serum total cholesterol as well as low-density and high-density lipoproteins. Y.S. was diagnosed with hyperlipidemia in 1989 and decided to not take lipid-lowering drugs but rather follow a lipid-lowering diet developed by a clinical registered dietician. The test results (discussed below) showed that initially, the lipid-lowering diet assisted in the achievement of healthy plasma triglyceride and total cholesterol levels. However, 8 years after commencement of the lipid-lowering diet (in 1997) Y.S. had his second diagnosis of hyperlipidemia. He then included a daily walking (no less than 10,000 steps per day, 5 to 6 times/week) and then replacing walking with indoor bike-peddling (minimum of 30 min, 5 times/week) exercise as part of his treatment plan and continued with his lipid-lowering diet.

(2) Interview

A face-to-face in-depth interview (using the recall method) was conducted that included assessment of the subject's medical history, lifestyle, exercise and dietary behavior before the introduction of the lipid-lowering diet as well as dietary behavior thereafter.

The interview initially examined the subject's diet (food preferences) before and after the adoption of the lipid-lowering diet. The subject was requested to choose the best suitable phrase among the idiomatic expressions (favorite; unfavorite; neither or both) for the following 12 items of foods or foodstuffs (beef; pork; chicken; whitefish; squid; seaweed including hijiki; mushrooms; fruit; eggs; cheese; udon noodles; ramen noodles). In addition, he was required to mark the best applicable value according to the following intake frequency scores (1 – eaten once a month; 2 – eaten a couple of times a month; 3 – eaten once a week; 4 – eaten a couple of times a week; and 5 – eaten daily) for each of the 12 items.

The interview then examined the subject's lifestyle and medical history, *i.e.*, smoking behavior (smoker or non-smoker including past smoker or complete non-smoker), smoking frequency (less than once a day, 1 to 2 times a day, 3 to 4 times a day, or almost every day), smoking consumption (per day or week and on what occasion), alcohol consumption behavior (non-drinker or ex-drinker or current drinker), frequency of alcohol consumption (less than once a week, 1 to 2 times a week, 3 to 4 times a week, or almost every day), alcohol consumption in amount (per day or week and on what occasion), personal medical history including familial disease, family and relative medical history. The subject's medical history was examined, including diagnosis of cardiovascular disease, cancer, and diabetes as well as familial hypertension, hyperlipemia and/or hypercholesterolemia. The interview then examined the specific details (mode, intensity and frequency) of the subject's exercise regimen (walking and indoor bike-peddling exercise). Finally, the subject was asked whether he had any additional information to provide that he thought was important for analysis.

(3) Calculation of BMI and approximation of LDL-cholesterol concentration

The subject's BMI (kg/m^2) was calculated. Approximation of low-density lipoprotein cholesterol (LDL-cholesterol) concentration and high-density lipoprotein cholesterol (HDL-cholesterol) concentration was made using Friedewald's equation [28], if such estimation was necessary.

LDL-cholesterol = (serum total cholesterol) – (HDL-cholesterol) – (triglycerides)/5

Results

(1) Body composition, blood pressure, lifestyle and lipids

Table 1 presents a summary of results from 1988 to 2011 for body weight, BMI, systolic and diastolic blood pressure, plasma triglycerides and serum total cholesterol.

The most recent data from a health checkup conducted on 22 August 2011 were included to demonstrate the subject's current demographic data and health status. On this date, the subject was 60 years old, 170.7 cm in stature, 61.8 kg in mass and had a BMI of 21.2 kg/m^2. His waist circumference was 77.4 cm and he had a systolic blood pressure of 124 mm Hg and a diastolic blood pressure of 78 mm Hg. Interestingly, the subject's blood pressure was consistently low to normal over the 20 years, demonstrating a range of 110-126 mm Hg for systolic and 67-80 mm Hg for diastolic blood pressure. His serum total cholesterol in 2011 was 183 mg/dL, HDL-cholesterol 46 mg/dL, LDL-cholesterol 121 mg/dL, triglycerides 62 mg/dL, and blood sugar (after a 12-hr fast) was 100 mg/dL.

In addition, from the interview it was determined that the subject: 1) was a non-smoker; 2) consumed a limited amount of alcohol; 3) had no history of familial disease (*i.e.*, familial hypercholesterolemia and familial hypertension); and 4) had no history of diagnosed hypertension, cardiovascular disease, cancer, and diabetes until the hyperlipidemia was diagnosed.

Table 1 demonstrates the high levels of plasma triglycerides and total serum cholesterol in 1989 and 1997 that led to the diagnosis of hyperlipidemia. In the meantime, the results from 1993 to 1997 suggest that: 1) there was a gradual increase in plasma triglyceride and serum total cholesterol despite continuing to follow the lipid-lowering diet; 2) the subject's weight stabilized around 68 to 69 kg compared with the baseline (2011) value (62 kg) and BMI was high, 23 to 24 kg/m^2, compared with the baseline value of 21 kg/m^2.

The table also suggests the positive effects of the subject's lifestyle modifications. Specifically, it seemed that the subject's initial employment of a lipid-lowering diet lowered plasma triglyceride and serum total cholesterol after the diagnosis of hyperlipidemia in 1989. For example, in 1991, 2 years after the commencement of the diet, levels of plasma triglyceride (97 mg/dL) and serum total cholesterol (192 mg/dL) were considerably lower than 1989 (triglyceride 124 mg/dL, cholesterol 265 mg/dL). However, eight years after commencement of the lipid-lowering diet the subject's annual health testing results in 1997 shows the high levels of plasma triglycerides and total serum cholesterol that led to his second diagnosis of hyperlipidemia. As above-mentioned, he then included a daily walking program (no less than 10,000 steps per day, 5 to 6 days/week) as part of his treatment plan and continued with his lipid-lowering diet. The combination of the lipid-lowering diet with the daily walking program seemed to be highly effective in maintaining healthy levels of plasma triglycerides and serum total cholesterol, even compared with the baseline values.

It is noted that the subject stopped the daily walking program in the period from 2004 to 2008 but continued consuming the lipid-lowering diet. By way of the cessation of an exercise program, the subject commenced an indoor bike-peddling exercise program

(minimum of 30 min of activity at least 5 days/week) instead of walking in 2008, because he was apprehensive about the rise in plasma triglycerides and total serum cholesterol. There was a re-introduction of exercise into the treatment program using bike-peddling exercise (instead of walking). This new regimen continued from 2008 to 2011. Table 1 illustrates how this new regimen could be effective with the subject achieving and maintaining a healthy level of plasma triglyceride, serum total cholesterol as well as low-density lipoprotein cholesterol.

Figure 1 is a representative diagram, in which the various trends in plasma triglyceride, serum total cholesterol and serum lipoprotein cholesterols (LDL- and HDL-cholesterol) from 1988 to 2011 are plotted. The figures suggest that the lipid-lowering diet had a greater impact on reducing total serum cholesterol than plasma triglycerides. Figure 1 then demonstrates how plasma triglycerides and total serum cholesterol increased again from 1991 despite the subject continuing the lipid-lowering diet. In 1997, the subject was diagnosed with hyperlipidemia again. Based on the interview, the subject indicated that his life was very stressful between 1991 and 1997. From Table 1 it can be seen that during this time there was a gradual increase in his weight and BMI in addition to the rise in plasma triglycerides and total serum cholesterol during this time.

The subject's second diagnosis of hyperlipidemia led to him adopting the walking program in combination with the lipid-lowering diet. As clearly seen in Figure 1, this new regimen was effective in reducing plasma triglycerides and total serum cholesterol as well as LDL-cholesterol; however, it had no effect on serum HDL-cholesterol. These results suggest that a lipid-lowering diet is not sufficient for maintaining low blood lipid levels, although it may be useful in the short term, and that an endurance exercise program should form part of a lipid-lowering intervention. This is highlighted by the finding that when the subject stopped exercising from 2004 to 2008 there was an increase in plasma triglycerides, total serum cholesterol and LDL-cholesterol.

(2) Lipid-lowering diet

Figure 2 demonstrates the subject's dietary behavior before and after the adoption of a lipid-lowering diet. There were three important findings. First, before adopting the lipid-lowering diet, the subject consumed food that was high in cholesterol, including eggs (egg-yolk), meats (particularly offal), and some shellfish (especially crabs, cuttlefish, and squid). Second, after the employment of the diet, the subject reduced his intake of the above food as well as his favorite foods that included fatty meat, cheese, and Chinese noodles (ramen; a particularly fat rich source). Finally, after the employment of the diet, the subject attempted to increase his consumption of a diet high in carbohydrate (udon noodles), high in cereal fiber (seaweed including hijiki and mushrooms), high in marine n-3 fatty acids (whitefish), and high in minerals and vitamins (fruits).

It is worthwhile to note that the subject participated in a project named the "Study of Daily Intakes of Fatty Acids, Sterols and Phospholipids by Japanese Men," in July 1996 where his dietary intake over a day (three meals including snacks) was analyzed. The research was conducted from May 1996 to December 1997 to estimate the quantity of fatty acids, sterols and phospholipids ingested by Japanese men (30-59 years of age) from their daily intake using the duplicate portion method [29]. From the analysis of the subject's

diet in the above study it was found that his daily intake of cholesterol was 169 mg/d, plant sterol = 238 mg/d, total fatty acid = 21 mg/d, saturated fatty acids = 5 mg/d, monounsaturated fatty acids = 8 mg/d, n-6 polyunsaturated fatty acids = 7 mg/d, and n-3 polyunsaturated fatty acids = 1 mg/d. In comparison, the average values for Japanese men his age [29] were: daily intake of cholesterol = 274.7 ± 135.9 mg/d, plant sterol = 164.1 ± 57.9 mg/d, total fatty acid = 41.3 ± 18.7 mg/d, saturated fatty acids = 28.9 ± 5.1 mg/d, monounsaturated fatty acids = 42.8 ± 4.8 mg/d, n-6 polyunsaturated fatty acids = 21.5 ± 6.9 mg/d, and n-3 polyunsaturated fatty acids = 6.8 ± 3.5 mg/d.

Although these findings was based on the analysis of a single day in 1996, the results suggest that the subject demonstrated a large reduction in daily cholesterol (61.5%) and total fatty acid (51%) intake compared with average intake for men in his age group. In addition, there was a large increase in the intake of plant sterols (145%) compared with the average. Despite the n-3 polyunsaturated fatty acid intake being low (1 mg/d) against the average (6.8 ± 3.5 mg/d), the results suggest that the subject's adoption of a lipid-lowering diet was beneficial.

Discussion

Several large-scale primary and secondary prevention trials have reported that cholesterol-lowering therapy can reduce the rate of the first occurrence and recurrence of CAD by about 20-40%. These studies confirmed primary and secondary prevention programs have cardiovascular benefits and reduce the occurrence of acute coronary syndromes across a wide age range [14-20]. For example, in the Scandinavian Simvastatin Survival Study [14], patients with preexisting CAD had a reduction in overall mortality of 30%, which was exclusively due to a 42% reduction in mortality from coronary causes, while there was a 27% reduction for all coronary events combined. However, it is an inescapable fact that pharmacological management (e.g. statins) of blood lipids is successful for preventing CAD. Although as mentioned previously, statins are costly, have side effects, and require medical supervision [21]. Recently, more attention paid to examining the effects of reducing lifestyle-related CAD risk factors for preventing CAD. The third revision of the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III) [30] emphasized, in addition to the importance of cholesterol control, the importance of other risk factors, associated with the metabolic syndrome, for development of cardiovascular disease, especially CAD. Specifically, metabolic syndrome in men was defined as the coexistence in an individual of at least three of the following: 1) waist girth over 102 cm; 2) serum triglyceride level over 150 mg/dL; 3) HDL-cholesterol level below 40 mg/dL; 4) systolic blood pressure over 130 mmHg and/or diastolic blood pressure over 85 mmHg; and 5) fasting plasma glucose level over 110 mg/dL.

Physicians typically supervise the treatment of hyperlipidemia and provide guidance regarding appropriate lipid-lowering medicine. Information will be provided about the future risk of hyperlipemia, the correlation between raised serum lipid levels and the incidence of CAD and atherosclerosis, and the need to take statins. In certain instances the physician will provide information about the need for lifestyle modifications to help lower serum cholesterol levels and prevent major fatal and non-fatal cardiovascular events. However, presently research comparing the effectiveness of statins versus lifestyle modifications

for reducing blood lipid levels and the primary and secondary prevention of CAD is limited. Therefore it is important that individuals with hyperlipidemia obtain sound advice regarding the different treatment options for lowering blood lipids.

In the present study, our primary aim was to determine whether a non-pharmacological program could be used to manage elevated blood lipid levels in a middle-aged individual recently diagnosed with hyperlipidemia. We examined 20 years of blood lipid data and related this to lifestyle modifications in order to answer the question regarding alternative treatments options for hyperlipidemia. Our analysis revealed the following important issues relating to the subject's modifications. First, the subject succeeded in altering his lifestyle through changing his diet and performing regular endurance exercise. Second, the lipid-lowering diet was ineffective for maintaining a long-term reduction in blood lipid. Third, walking or bike-peddling exercise plus a lipid-lowering diet were effective in reducing plasma triglycerides, total serum cholesterol and LDL-cholesterol but had no effect on serum HDL-cholesterol. In conclusion, the use of a combination of a lipid-lowering diet and physical aerobic exercise (walking or bike-peddling exercise) was shown to be highly effective for achieving healthy serum cholesterol in a male with a predisposition for developing hyperlipidemia. In this regard, it seems that promoting lifestyle modifications should be the first option before prescription of statins, even though physicians currently prescribe appropriate lipid-lowering medicine with lifestyle modifications as the first-line treatment in the primary prevention against CAD.

Conclusions

The results suggest that lifestyle modifications such as those used by the subject in the present study have an important role to play in the primary prevention and treatment of hyperlipidemia. Promoting lifestyle modifications should be the first option before prescription of statin for every physician supervising patients with hyperlipidemia as well as in the primary prevention against CAD.

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Table 1. Overview of the object's blood test data enrolled from the 1988's annual health checkup to the 2011's, focusing on weight (body weight), BMI (body mass index), blood pressure (systolic and diastolic), plasma neutral fat and serum total cholesterol.

Annual health checkup	1988's	1989's	1991's	1993's	1997's	2000's	2002's	2004's	2006's	2008's	2011's
Body weight (Kg)	63.0	66.0	68.5	69.0	68.0	64.3	63.3	66.6	65.5	64.1	61.8
BMI (Kg/m^2)	21.3	22.4	23.4	23.6	23.3	22.0	21.6	22.9	22.6	22.2	21.2
Blood pressure (mmHg)											
Systolic	122	116	112	118	120	125	116	120	115	126	124
Diastolic	80	72	70	76	72	73	72	74	78	72	78
Plasma triglycerides (mg/dL)	72	124	97	127	168	79	68	44	61	105	62
Serum total cholesterol (mg/dL)	217	265	192	234	275	207	192	199	216	226	183

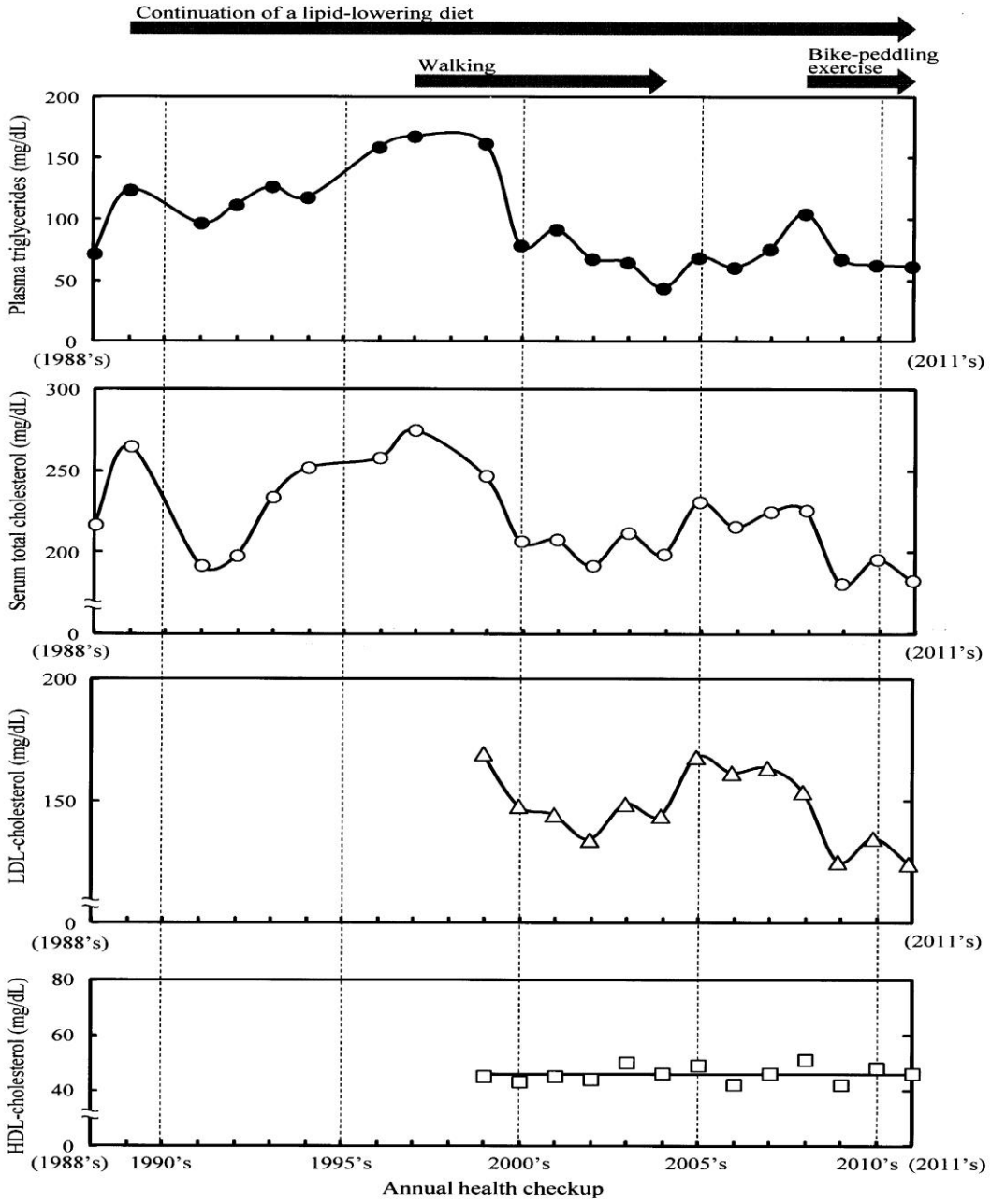

Figure 1. Plasma triglyceride, total serum cholesterol, LDL- and HDL-cholesterol levels plotted against time (1988 to 2011). The figure demonstrates when the lipid-lowering diet was started as well as the time-points when walking exercise was started and stopped (2004–2008) and when there was a re-introduction of exercise into the treatment program using bike-peddling exercise (instead of walking).

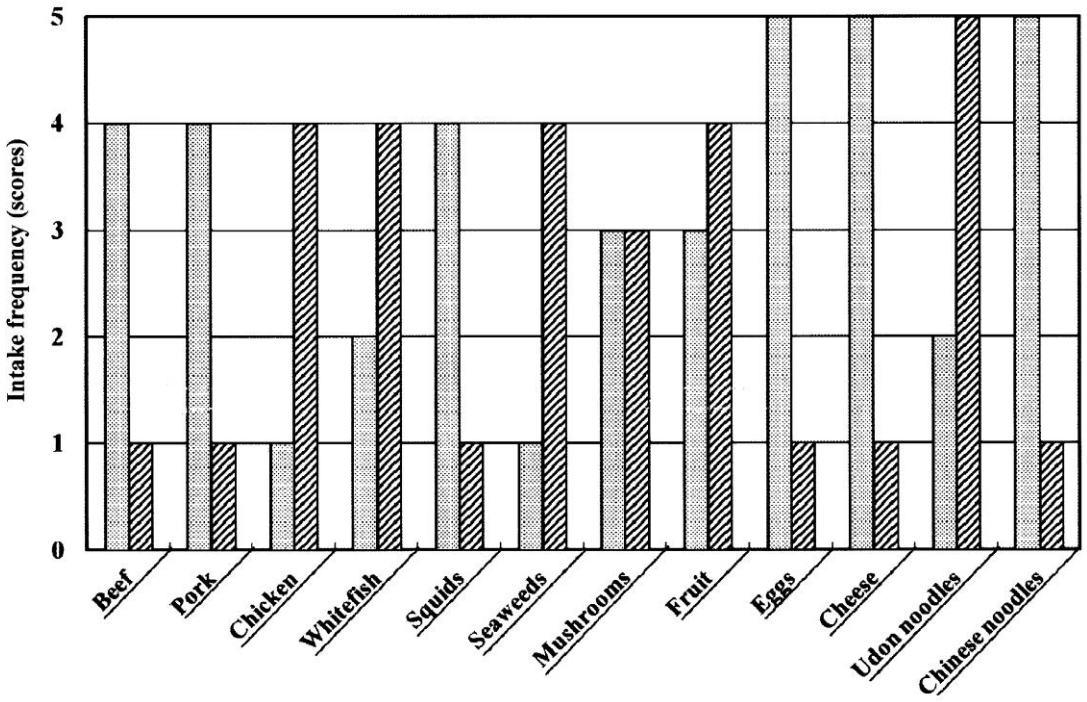

Figure 2. Comparison of the subject's food preferences before and after the adoption of a lipid-lowering diet. The assessment was conducted twice: once before the lipid-lowering diet (dotted bars) and once after the diet (diagonal shaded bars). The ordinate exhibits the applicable threshold values (scores of specific food intake frequency) before and after adopting the lipid-lowering diet: 1 – eaten once a month; 2 – eaten a couple of times a month; 3 – eaten once a week; 4 – eaten a couple of times a week; and 5 – eaten daily.