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Long-Term Low-Calorie Low-Protein Vegan Diet and Endurance Exercise are Associated with Low Cardiometabolic Risk

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ABSTRACT

***Background*: Western diets, which typically contain large amounts of energy-dense processed foods, together with a sedentary lifestyle are associated with increased cardiometabolic risk. We evaluated the long-term effects of consuming a low-calorie low-protein vegan diet or performing regular endurance exercise on cardiometabolic risk factors. *Methods*: In this cross-sectional study, cardiometabolic risk factors were evaluated in 21 sedentary subjects, who had been on a low-calorie low-protein raw vegan diet for 4.4 ± 2.8 years, (mean age, 53.1 ± 11 yrs), 21 body mass index (BMI)-matched endurance runners consuming Western diets, and 21 age- and gender-matched sedentary subjects, consuming Western diets. *Results*: BMI was lower in the low-calorie low-protein vegan diet (21.3 ± 3.1 kg/m^2) and endurance runner (21.1 ± 1.6 kg/m^2) groups than in the sedentary Western diet group (26.5 ± 2.7 kg/m^2) ($p < 0.005$). Plasma concentrations of lipids, lipoproteins, glucose, insulin, C-reactive protein, blood pressure (BP), and carotid artery intima-media thickness were lower in the low-calorie low-protein vegan diet and runner groups than in the Western diet group (all $p < 0.05$). Both systolic and diastolic BP were lower in the low-calorie low-protein vegan diet group (104 ± 15 and 62 ± 11 mm Hg) than in BMI-matched endurance runners (122 ± 13 and 72 ± 9 mmHg) and Western diet group (132 ± 14 and 79 ± 8 mm Hg) ($p < 0.001$); BP values were directly associated with sodium intake and inversely associated with potassium and fiber intake. *Conclusions*: Long-term consumption of a low-calorie low-protein vegan diet or regular endurance exercise training is associated with low cardiometabolic risk. Moreover, our data suggest that specific components of a low-calorie low-protein vegan diet provide additional beneficial effects on blood pressure.**

INTRODUCTION

DURING THE LAST 50 YEARS, populations living in industrialized countries have experienced considerable changes in dietary and physical activity behaviors, including increased consumption of highly refined carbohydrates, salt, and processed foods, decreased intake of phytochemicals embedded in the fiber matrix of vegetables, beans, fruits and grains, and decreased physical activity.[1,2] It has been hypothesized that these lifestyle changes have

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contributed to the recent increase in risk factors for coronary heart disease (CHD), including obesity, type 2 diabetes, dyslipidemia, hypertension, and the metabolic syndrome.[3]

It is difficult to evaluate the effect of lifestyle modification on CHD risk factors by using the gold standard of randomized controlled trials, because of poor long-term adherence to changes in dietary intake and physical activity.[4] However, studying specific populations who have successfully made long-term lifestyle modifications could provide important insights into the potential efficacy of diet and endurance exercise in reducing cardiometabolic risk. We have identified two groups of middle-aged men and women who have made sustained changes in either dietary intake or physical activity; one group has markedly reduced their intake of refined foods by eating unprocessed plant-based foods, and the other group has increased their physical activity by participating in regular endurance exercise.

The purpose of the present study was to evaluate the relationships between long-term consumption of a low-calorie low-protein vegan diet, long-term regular endurance exercise, and major metabolic risk factors for CHD. Blood pressure, plasma cardiometabolic risk factors (lipids, lipoprotein cholesterol, glucose, insulin, and C-reactive protein [CRP]), and common carotid artery intima-media thickness (IMT) were determined in middle-aged adults who were: (1) consuming a low-calorie low-protein vegan diet, (2) endurance runners matched on body mass index (BMI) with the low-calorie low-protein vegan group, or (3) nonobese sedentary subjects consuming typical Western diets. We hypothesized that a low-calorie low-protein vegan diet, regular endurance exercise, and decreased adiposity would be associated with a beneficial effect on cardiometabolic risk.

SUBJECTS AND METHODS

Subjects

Three groups of subjects (21 subjects per group consisting of 13 men and 8 women) participated in this study. One group of subjects was recruited by contacting The St. Louis Vegetarian Society and a Raw Food online magazine (*Raw Food News*, www.rawfoods newsmagazine.com). These subjects were consuming a low-calorie low-protein vegan diet, composed of unprocessed and uncooked plant-derived foods, for at least 2 years (mean 4.4 $\pm$ 2.8 years; range, 2–10 years). Subjects were excluded from the low-calorie low-protein vegan diet group if they ate: (1) animal products including meat, diary, and eggs and (2) cooked and processed foods. The second group of subjects comprised endurance runners who were matched with the low-calorie low-protein vegan diet group on age, gender, and BMI, and were recruited by contacting local running clubs. These subjects participated in regular endurance running exercise, and ran an average of 48 miles per week (range, 20–90 miles per week) for an average of 21 years (range, 5–35 yrs). Subjects were excluded from the exercise group if they did not perform at least 20 miles of running per week for the 24 months prior to the study. The third group of subjects were healthy, sedentary nonobese (BMI $< 30\ kg/m^2$) subjects, who were eating typical Western diets. These subjects were recruited by local advertising and were matched with the low-calorie low-protein vegan diet group on age, gender, and height. No subject consuming a low-calorie low-protein vegan diet was taking vitamin or mineral supplements, whereas many of the subjects in the other groups were taking supplements, ranging from one multivitamin per day to combinations of vitamins, antioxidants, selenium, and folate.

The characteristics of the study subjects are shown in Table 1. All subjects underwent a comprehensive medical evaluation, including a medical history, physical examination, routine blood tests, and urinalysis. None of the subjects had evidence of chronic disease, including cardiovascular, lung, gastrointestinal, autoimmune diseases, type 2 diabetes, or cancer, and none smoked tobacco. In addition, no subject was taking hormone replacement therapy, or other medications that could have affected the outcome variables. All subjects were weight stable (i.e., reported less than a 2 kg weight change for at least 6 months before the study). The low-calorie low-protein vegan diet and

Table 1. Characteristics of the Study Subjects

	Low-calorie low-protein vegan diet group (n = 21)	*Endurance runner group* (n = 21)	*Western diet group* (n = 21)	p *value*
Age (yrs)	53.1 ± 11	53.2 ± 10	53.1 ± 9	NS
Height (m)	1.72 ± 0.1	1.72 ± 0.1	1.73 ± 0.1	NS
Weight (kg)	63.1 ± 10.1[a]	63.1 ± 9.6[b]	79.5 ± 10.5	0.0001
BMI (kg/m^2)	21.3 ± 3.1[a]	21.1 ± 1.6[b]	26.5 ± 2.7	0.0001
Body fat (% body weight)				
Men	13.7 ± 2.8[a,c]	9.2 ± 4.2[b]	21.0 ± 7.1	0.0001
Women	26.9 ± 8.3[a]	20.9 ± 6.5[b]	42.3 ± 5.3	0.0001
Lean body mass (kg)				
Men	53.2 ± 5.6	59.2 ± 5.6	58.1 ± 9.2	NS
Women	40.1 ± 5.3	38.9 ± 4.7	41.8 ± 4.5	NS

Values are means ± standard deviation (SD).
[a,b]Significantly different from Western diet group: [a]$p \leq 0.002$, [b]$p = 0.0001$.
[c]Significantly different from Endurance runner group: $p \leq 0.05$.

Western diet subjects were sedentary (regular endurance exercise less than 1 hour per week). Five women in the low-calorie low-protein vegan diet group, four in the endurance runners group, and seven in the sedentary Western diet group were postmenopausal.

This study was approved by the Human Studies Committee and the General Clinical Research Center Scientific Advisory Committee of Washington University School of Medicine. All subjects gave informed consent before their participation.

Study protocol

Dietary assessment. Subjects were instructed by a research dietitian to record all food and beverage intake, including preparation methods and portion sizes, for 7 consecutive days. Measuring spoon and cup sets, and food diaries with a ruler imprinted on the back cover were provided to the participants to assist with portion size determinations. Food records were analyzed by using the NDS-R program (version 4.03_31), which is the Nutrition Data System for research from the Nutrition Coordinating Center at the University of Minnesota.[5] Supplements were not included in the diet records and in the resulting nutrient analysis.

Assessment of risk factors for CHD. Subjects were admitted to the outpatient facilities of General Clinical Research Center at Washington University School of Medicine in the morning after they had fasted for 12 hours overnight. Height was measured without shoes to the nearest 0.1 cm. Body weight was obtained on a balance scale in the morning. Total body fat mass and lean body mass were determined by using dual-energy x-ray absorptiometry (QDR 1000/w, Hologic, Waltham, MA), as described by Salamone et al.[6] Blood pressure was measured by using a mercury sphygmomanometer, while subjects were sitting upright, with the cuff at the level of the heart, after 15 minutes of rest in a quiet environment. Cuff size was selected based on a measurement of the arm circumference. The average of four systolic and diastolic BP measurements taken at approximately 5-minute intervals was used to determine BP values. A venous blood sample was obtained to determine serum glucose, lipids, lipoproteins, CRP, and insulin concentrations.

Measurement of carotid artery IMT. Carotid artery IMT, which correlates with coronary artery atherosclerosis,[7] was determined by using high-resolution, real-time B-mode ultrasonography with an 11-MHz transducer to image the right and left common carotid arteries. Arteries were scanned in the longitudinal projections over an arterial segment that included 30 mm of the distal common carotid artery.[8] IMT was measured in the anterior wall of the vessel as the distance from the trailing edge of the adventitia to the leading edge of the intima-

media; and in the posterior wall of the vessel as the distance from the leading edge of the intima-media to the trailing edge of the adventitia. The average of 16 measurements was taken as the mean IMT. Examinations and image analyses were performed by a trained sonographer who was not aware of subjects' dietary habits.

Sample analyses. Measurement of serum lipid and lipoprotein concentrations was performed in the Core Laboratory for Clinical Studies at Washington University. Total cholesterol (T-CHOL) and glycerol-blanked triacylglycerols were measured by using an automated enzymatic commercial kits (MilesTechnicon, Tarrytown, NY). High-density lipoprotein cholesterol (HDL-C) was measured in plasma after precipitation of apolipoprotein B-containing lipoproteins by dextran sulfate (50,000 MW) and magnesium. Low-density lipoprotein cholesterol (LDL-C) was calculated by using the Friedewald equation. These methods are continuously standardized by the Lipid Standardization Program of the Centers for Disease Control and Prevention. CRP was measured by using a highly sensitive enzyme-linked immunosorbent assay (ELISA) kit (American Laboratory Products Company Diagnostics, Windham, NH). Plasma glucose was measured by the glucose oxidase method (Beckman Instruments, Fullerton, CA), and insulin was measured by radioimmunoassay. Insulin resistance was calculated by using homeostasis model assessment (HOMA) (HOMA-IR = [fasting glucose {mmol/l} $\times$ fasting insulin {μU/mL]/22.5).[9]

Statistical analyses

One-way analysis of variance (ANOVA) was used to compare group variables followed by Tukey post-hoc testing where indicated. One-way ANOVA with Games-Howell was performed for distributions where equal variances could not be assumed. Pearson correlation was used to assess associations between continuous variables. Statistical significance was set at $p < 0.05$ for all tests. All data were analyzed by using SPSS FOR WINDOWS software, version 13.0 (SPSS Inc., Chicago, IL). All values are expressed as means $\pm$ standard deviation (SD).

RESULTS

Nutrient intake

Subjects consuming a low-calorie low-protein vegan diet ate a wide variety of uncooked sprouted grains and beans, nuts, seeds, vegetables, fruits, and olive oil, and strictly avoided processed and refined foods (e.g.,partially hydrogenated oils, refined flours, sweets, simple sugars, soft-drinks), and foods of animal origin. Daily sodium intake was significantly lower in the low-calorie low-protein vegan diet group than in both the endurance runners and Western diet groups (Table 2). Total fat, monounsaturated and polyunsaturated fatty acids (MUFA; PUFA) intakes, expressed as a percent of total energy intake, were significantly higher in the low-calorie low-protein vegan diet group than in both the endurance runners and Western diet groups, whereas relative saturated fatty acid (SFA) intake was significantly lower in the low-calorie low-protein vegan diet group than in the Western diet group (Table 2). Daily dietary total fiber (both soluble, and insoluble fiber) intake in the low-calorie low-protein vegan diet group was significantly higher than their intakes in the endurance runners or Western diet groups (Table 2). Endurance runners and Western diet subjects ate typical Western diets, containing foods of both plant and animal origin. Daily intake of total trans-fatty acids were similar in the endurance runners and Western diet group, which were much higher than in the low-calorie low-protein vegan diet group (Table 2).

Body composition

Body mass index and percent body fat were significantly lower in the low-calorie low-protein vegan diet and endurance runners groups than in the Western diet group (Table 1). Percent body fat tended to be lower in the endurance runners group than in the low-calorie low-protein vegan diet group, but the difference was statistically significantly different only in men (Table 1).

Table 2. Macronutrient and Micronutrient Intake Among Groups of Study Subjects

Dietary components	*Low-calorie low-protein vegan diet group* (n = *18*)	*Endurance runners group* (n = *20*)	*Western diet group* (n = *18*)	p *value*
Energy (kcal/d)	1989 ± 556[a]	2634 ± 700	2346 ± 558	0.018
Carbohydrate (% of energy)	47.8 ± 6.5[a]	54.2 ± 9.4	48.8 ± 6.0	0.01
Protein (% of energy)	9.3 ± 3.3[a,b]	15.3 ± 3.0	17.0 ± 3.5	0.0001
Protein (g/kg/d)	0.73 ± 0.2[a,b]	1.60 ± 0.4	1.23 ± 0.4	0.0001
Fat (% of energy)	42.8 ± 8.2[a,b]	30.5 ± 9.0	34.2 ± 6.4	0.0001
SFA (% of energy)	7.7 ± 4.4[b]	9.6 ± 3.6	11.5 ± 3.0	0.013
MUFA (% of energy)	21.1 ± 4.1[a,b]	11.9 ± 3.8	12.8 ± 2.6	0.0001
PUFA (% of energy)	10.9 ± 4.6[a,b]	6.6 ± 2.3	7.1 ± 2.1	0.0001
TRANS-FA (g/d)	0.4 ± 0.7[a,b]	5.3 ± 2.6	5.9 ± 2.6	0.0001
Total fiber (g/d)	51.1 ± 20[a,b]	29 ± 15	22 ± 8	0.0001
Potassium (g/d)	5.5 ± 1.9[a,b]	3.5 ± 1.3	3.4 ± 1.1	0.0001
Sodium (g/d)	1.4 ± 0.8[a,b]	3.7 ± 1.2	3.7 ± 1.2	0.0001

All values are means ± standard deviation (SD).
[a]Significantly different from endurance runners, $p \leq 0.05$.
[b]Significantly different from Western diet group, $p \leq 0.05$.
SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; TRANS-FA, total trans-fatty acids.

Lipids and lipoproteins

Plasma total cholesterol, LDL-C, triglycerides concentrations and the T-CHOL:HDL-C ratio were lower in the low-calorie low-protein vegan diet and endurance runner groups than in the Western diet group (Table 3). Plasma HDL-C concentration was higher in the endurance runner group than in the Western diet and the low-calorie low-protein vegan diet groups, but only the difference between endurance runners and the Western diet group was statistically significant (Table 3).

Systolic and diastolic blood pressure

Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were lower in the low-calorie low-protein vegan diet group than in the endurance runners and the Western diet group (Table 4). SBP and DBP tended to be lower in the endurance runners than in the Western diet groups but the difference was only statistically significant for DBP (Table 4). SBP correlated directly with sodium intake ($r = 0.477$, $p = 0.0001$), and was inversely correlated with total fiber ($r = 0.441$,

Table 3. Lipids and Lipoproteins Among the Groups of Study Subjects

	Low-calorie low-protein vegan diet group (n = *21*)	*Endurance runner group* (n = *21*)	*Western diet group* (n = *21*)	p *value*
T-CHOL (mg/dL)	143 ± 23[a]	161 ± 27[b]	187 ± 33	0.0001
LDL-C (mg/dL)	76 ± 23[a]	84 ± 19[b]	112 ± 29	0.0001
HDL-C (mg/dL)	56 ± 13	65 ± 17[b]	52 ± 11	0.008
T-CHOL/HDL-C ratio	2.7 ± 0.7[a]	2.6 ± 0.5[a]	3.7 ± 0.9	0.0001
Triglycerides (mg/dL)	56 ± 37[a]	62 ± 17[a]	120 ± 59	0.0001

Values are means ± standard deviation (SD).
[a]Significantly different from Western diet group, $p = 0.0001$.
[b]Significantly different from Western diet group, $p \leq 0.02$.
T-CHOL, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Table 4. Blood Pressure, Insulin Sensitivity, CRP, and IMT Among the Groups of Study Subjects

	Low-calorie low-protein vegan diet group (n = 21)	*Endurance runner group* (n = 21)	*Western diet group* (n = 21)	p *value*
SBP (mm Hg)	104 ± 15[a,c]	122 ± 13	132 ± 14	0.0001
DBP (mm Hg)	62 ± 11[b,c]	72 ± 9[f]	79 ± 8	0.0001
Fasting glucose (mg/dL)	85 ± 7[c]	88 ± 6[f]	95 ± 6	0.0001
Fasting insulin (μU/mL)*	2.8 ± 2[g]	2.1 ± 2[d]	5.9 ± 4	0.0001
HOMA-IR	0.59 ± 0.43[c]	0.45 ± 0.38[d]	1.36 ± 0.83	0.0001
hsCRP (mg/L)*	0.52 ± 0.6[e]	0.75 ± 0.9[e]	2.61 ± 3.3	0.003
Carotid artery IMT (mm)	0.56 ± 0.1[c]	0.63 ± 0.1[e]	0.74 ± 0.1	0.0001

Values are means ± standard deviation (SD).

[a,b]Significantly different from endurance runners group, [a]$p = 0.0001$; [b]$p = 0.001$.

[c,d,e,f,g]Significantly different from Western diet group, [c,d]$p = 0.0001$; [e]$p \leq 0.05$; [f,g]$p \leq 0.006$.

*Plasma fasting insulin and CRP concentration data have been published previously in a paper dealing with metabolic cancer risk factors.[10]

CRP, C-reactive protein; IMT, intima-media thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA-IR, homeostasis model assessment-insulin resistance.

$p = 0.0001$) (Fig. 1) and potassium ($r = 0.492$, $p = 0.0001$; Fig. 2) intake. DBP also correlated directly with sodium intake ($r = 0.464$, $p = 0.0001$) (Fig. 2), and was inversely correlated with total fiber ($r = 0.474$, $p = 0.0001$; Fig. 1) and potassium ($r = 0.460$, $p = 0.0001$; Fig. 2) intake. These correlations were based on data from all groups combined.

Insulin sensitivity and CRP

Plasma fasting glucose and insulin concentrations, and insulin resistance, assessed by HOMA-IR index, were lower in the low-calorie low-protein vegan diet and endurance runners groups than in the Western diet group (Table 4). Plasma CRP concentration was also

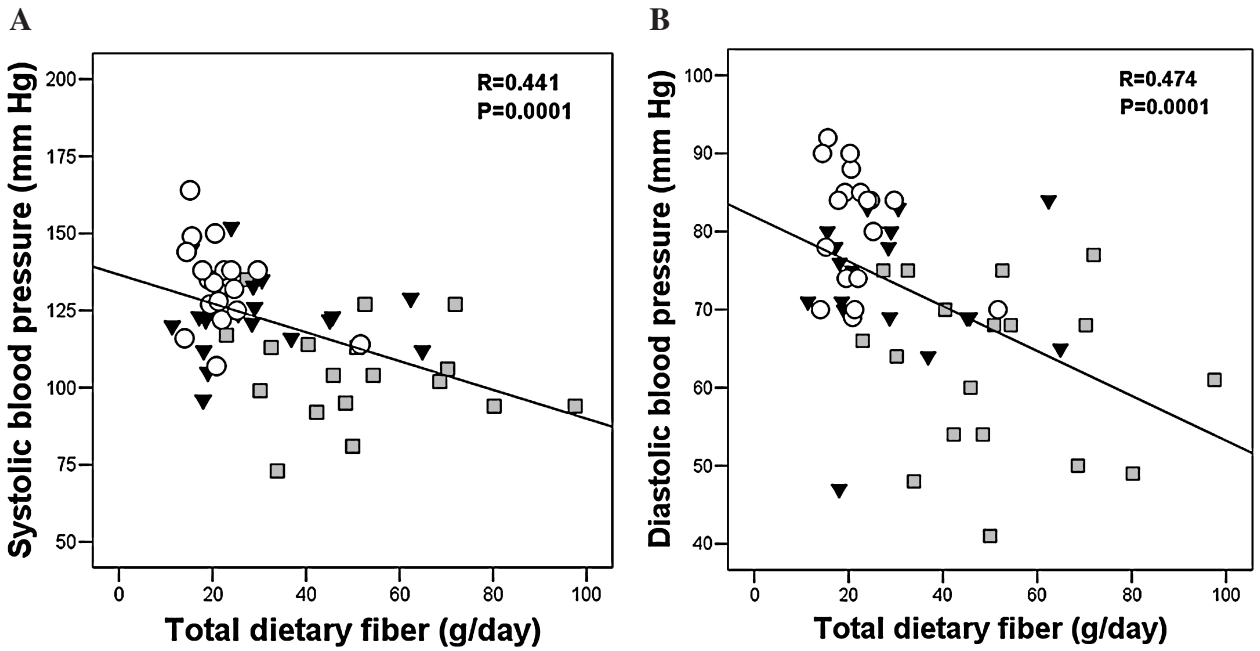

FIG. 1. Relationship between total dietary fiber intake and systolic blood pressure (SBP) values (**A**) and diastolic blood pressure (DBP) values (**B**).

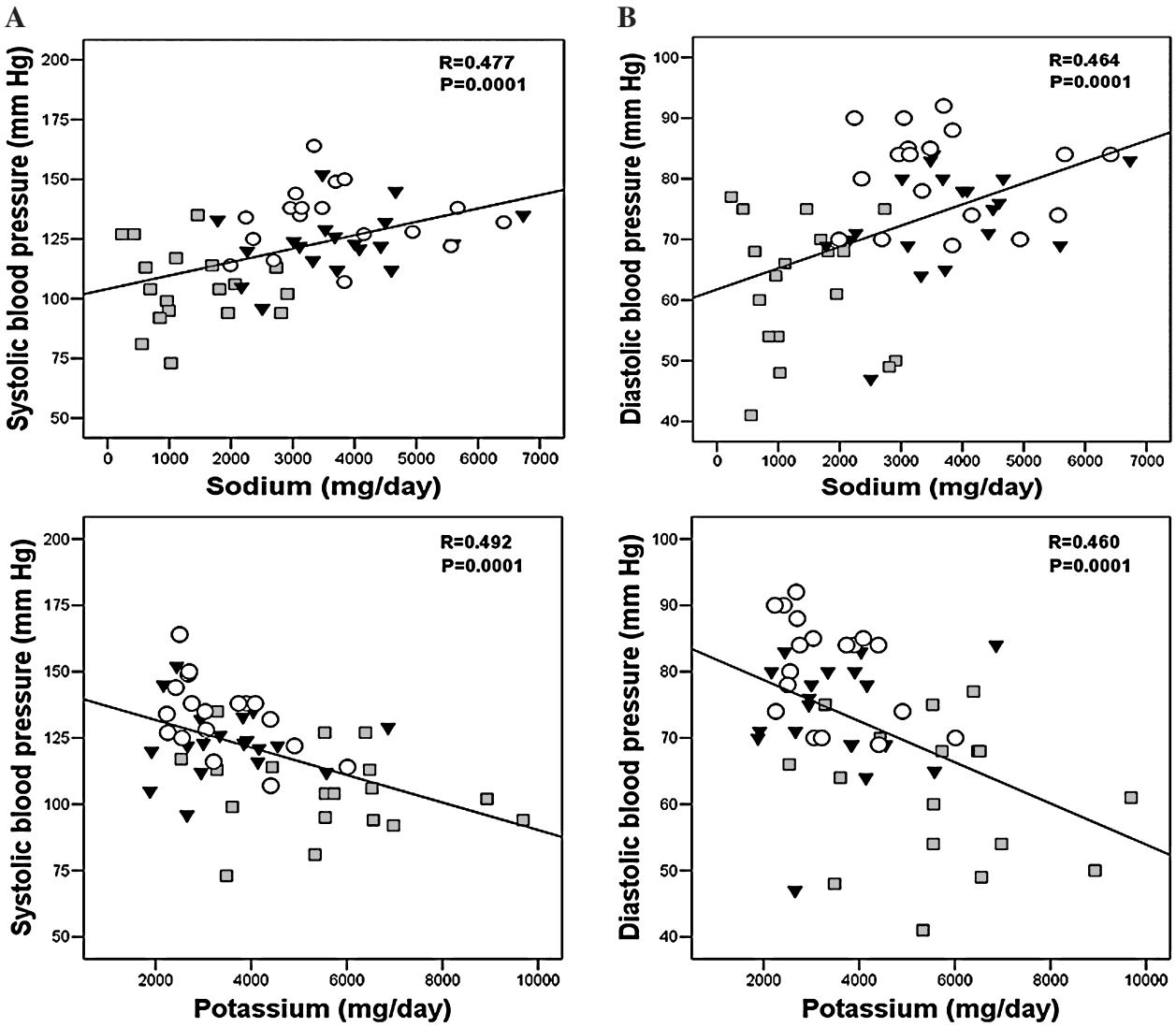

FIG. 2. Relationship between dietary sodium and potassium concentration and systolic blood pressure (SBP; **A**), and diastolic blood pressure (DBP; **B**).

lower in the low-calorie low-protein vegan diet and endurance runners groups than in the Western diet group (Table 4). Plasma fasting insulin and CRP concentration data have been published previously in a manuscript dealing with metabolic cancer risk factors.[10]

Carotid IMT

Common carotid artery IMT was lower in the low-calorie low-protein vegan diet and endurance runners groups than in the Western diet group (Table 4). No subject in either group had evidence of atherosclerotic plaque, defined as an IMT of more than 1.0 mm and an increase of at least 100% compared to an adjacent wall segment.

DISCUSSION

The data from the present study demonstrate that consuming a low-calorie low-protein vegan diet or participating in regular endurance exercise training is associated with a decrease in cardiometabolic risk. Plasma concentrations of lipids, lipoproteins, glucose, insulin, CRP, BP, and IMT of the common carotid arteries were lower in subjects consuming a low-calorie low-protein vegan diet and in subjects who were endurance runners than in nonobese sedentary subjects who were consuming typical Western diets. This suggests that leanness is largely responsible for the reduced car-

diometabolic risk. However, subjects eating a low-calorie low-protein vegan diet had much lower SBP and DBP values than BMI-matched endurance runners who were consuming a Western diet. These results support the notion that long-term lifestyle modifications in either diet or physical activity that result in leanness improve multiple metabolic risk factors for CHD, and suggest that dietary factors can provide additional beneficial effects on BP.

High blood pressure is a major risk factor for cardiovascular disease.[11] Data from large population studies indicate that death from both CHD and stroke increase progressively from systolic and diastolic blood pressure values of 115 mm Hg and 75 mm Hg, respectively.[12] Therefore, maintaining a blood pressure that is 15%–20% below the upper limit of normal is likely to have clinical benefits. Body composition is an important component of BP homeostasis.[13] Obesity is associated with increases in both systolic and diastolic BP,[14] and weight loss decreases BP.[15] For example, a 10-kg weight loss sustained for 2 years causes a 6.0 mm Hg and 4.6 mm Hg reduction in systolic and diastolic BP in overweight and obese adults.[16] Accordingly, our data show that persons who maintain a low body fat mass by either consuming a low-calorie low-protein vegan diet or by exercising had lower BP values than nonobese sedentary subjects consuming typical Western diets. Moreover, our findings suggest that specific dietary components can have additional beneficial effects on BP, independent of body fat mass. Systolic and diastolic BP values were approximately 15% lower in the low-calorie low-protein vegan diet group (approximately 19% body weight from fat) than in the BMI-matched lean distance runners (approximately 14% body weight from fat). The mechanism for this effect could be related to fiber (or phytochemicals embedded in the fiber matrix), sodium, and potassium intakes, which have been shown to affect blood pressure in previous studies.[17–20] In our subjects, systolic and diastolic BP correlated directly with sodium intake, and was inversely correlated with potassium and fiber intake. Our low-calorie low-protein vegan diet group consumed approximately twice as much fiber, 60% less sodium and 60% more potassium daily than endurance runners and sedentary subjects consuming typical Western diets.

Despite markedly different diets and levels of physical activity, most of the risk factors for atherosclerosis were similarly low in the low-calorie low-protein vegan diet and endurance exercise groups. This suggests that the effect that a low-calorie low-protein vegan diet and endurance training have in common, a low BMI, is largely responsible for the reduced cardiometabolic risk, and in particular for the reductions in serum glucose and insulin, CRP and triglyceride concentrations and HOMA-IR index. However, there were some interesting differences in the lipoprotein profile. Although the ratio of T-CHOL:HDL-C was similarly low in the low-calorie low-protein vegan diet group and in the exercisers, serum T-CHOL concentration tended to be lower in the low-calorie low-protein vegan diet group, while serum HDL-C concentration tended to be higher in the exercisers. Endurance exercise training is known to raise HDL-C.[21] On the other hand, our results suggest that a low-calorie low-protein vegan diet is more effective than exercise training in lowering serum T-CHOL concentration, even in the face of a high fat diet (approximately 43% of the calories from fat).

Effective prevention and therapy of obesity has been difficult to achieve by using lifestyle interventions.[22] We found that sedentary subjects who chose to consume a low-calorie low-protein vegan diet rich in unrefined and unprocessed foods had a lower body fat mass than sedentary subjects who chose to consume an *ad libitum* Western diet. Our study cannot determine the precise mechanism(s) responsible for the differences in energy intake between groups. However, specific components of a low-calorie low-protein vegan diet itself, specifically low-energy-density[23,24] and high-fiber[25] foods, could influence total energy intake. Data from several studies suggest that consuming a low-energy-density diet[26–28] and high-fiber foods[29] decrease total energy intake and induce weight loss. These findings might also be relevant to human aging, as it has been shown that calorie restriction slows aging, and prevents or attenuates the severity of chronic diseases in different species, including yeast, flies, worms, fish, and rodents.[30] Moreover, it

has been shown that long-term calorie restriction has beneficial effects on left ventricular diastolic function, a marker of primary aging, in mice and humans.[31,32]

Our study has several limitations. First, because of the cross-sectional design of our study, we are only able to show associations with diet, physical activity, and CHD risk factors, and cannot determine true causal relationships. A long-term randomized controlled trial would be needed to determine cause-and-effect relationships. However, this type of trial would be extremely difficult to perform, because of the difficulty in achieving long-term dietary and exercise compliance. Second, our study evaluated risk factors associated with CHD, but did not evaluate the prevalence of CHD itself. It is not known if these surrogate markers will reflect the incidence of CHD in our study subjects. Finally, the small sample size and the cross-sectional nature of this study do not allow us to exclude that other unknown factors could play a role in the reported differences. However, the observations made in this study are a first-step in elucidating the effects of consuming a low-calorie low-protein vegan diet and performing regular endurance exercise on CHD risk factors in human subjects.

The results of the present study show that long-term consumption of a low-calorie low-protein vegan diet or regular endurance exercise training is associated with a decrease in multiple risk factors for CHD. Moreover, eating a low-calorie low-protein vegan diet, which is low in sodium and high in fiber and potassium, might have greater beneficial effects on blood pressure than endurance exercise, independent of adiposity.

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Luigi Fontana participated in the concept, design, and implementation of the study, undertook plausibility testing, and drafted the report. Timothy E. Meyer participated in the collection and analyses of the data and in the drafting of the report. Samuel Klein participated in the design and in the drafting of the report. John O. Holloszy participated in the design, implementation of the study, and drafting of the report. All authors declared that they participated in the study as mentioned above and that they reviewed and approved the manuscript in its final version.

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