Effects of the Dietary Approaches to Stop Hypertension Diet Alone and in Combination With Exercise and Caloric Restriction on Insulin Sensitivity and Lipids

James A. Blumenthal, Michael A. Babyak, Andrew Sherwood, Linda Craighead, Pao-Hwa Lin, Julie Johnson, Lana L. Watkins, Jenny T. Wang, Cynthia Kuhn, Mark Feinglos, Alan Hinderliter

Abstract—This study examined the effects of the Dietary Approaches to Stop Hypertension (DASH) diet on insulin sensitivity and lipids. In a randomized control trial, 144 overweight (body mass index: 25 to 40) men (n=47) and women (n=97) with high blood pressure (130 to 159/85 to 99 mm Hg) were randomly assigned to one of the following groups: (1) DASH diet alone; (2) DASH diet with aerobic exercise and caloric restriction; or (3) usual diet controls (UC). Body composition, fitness, insulin sensitivity, and fasting lipids were measured before and after 4 months of treatment. Insulin sensitivity was estimated on the basis of glucose and insulin levels in the fasting state and after an oral glucose load. Participants in the DASH diet with aerobic exercise and caloric restriction condition lost weight (−8.7 kg [95% CI: −2.0 to −9.7 kg]) and exhibited a significant increase in aerobic capacity, whereas the DASH diet alone and UC participants maintained their weight (−0.3 kg [95% CI: −1.2 to 0.5 kg] and +0.9 kg [95% CI: 0.0 to 1.7 kg], respectively) and had no improvement in exercise capacity. DASH diet with aerobic exercise and caloric restriction demonstrated lower glucose levels after the oral glucose load, improved insulin sensitivity, and lower total cholesterol and triglycerides compared with both DASH diet alone and UC, as well as lower fasting glucose and low-density lipoprotein cholesterol compared with UC. DASH diet alone participants generally did not differ from UC in these measures. Combining the DASH diet with exercise and weight loss resulted in significant improvements in insulin sensitivity and lipids. Despite clinically significant reductions in blood pressure, the DASH diet alone, without caloric restriction or exercise, resulted in minimal improvements in insulin sensitivity or lipids. (*Hypertension*. 2010; 55:1199-1205.)

Key Words: diet ∎ hypertension ∎ lipids ∎ insulin resistance ∎ exercise

High blood pressure (BP; HBP) affects >70 million Americans and is among the most common reasons for outpatient visits to physician offices.[1] Although HBP can be lowered pharmacologically,[2,3] antihypertensive medications may be costly, oftentimes must be used in combination to achieve adequate BP control, and can be associated with adverse effects that impair quality of life and reduce adherence.[2,4] Moreover, metabolic abnormalities associated with HBP, such as insulin resistance and hyperlipidemia, may persist or may be exacerbated by some medications.[5] Consequently, there is great deal of interest in the use of nonpharmacologic interventions in the prevention and management of HBP.

The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC)[6] recommends that lifestyle modifications, such

as weight loss and regular aerobic exercise, be the initial treatment strategy for lowering HBP and specifically recommends the Dietary Approaches to Stop Hypertension (DASH) diet, a diet rich in fiber, fruits, vegetables, and low-fat dairy products that is also low in fat. This diet was established as efficacious in reducing BP in a series of 4- to 8-week "feeding" trials, in which HBP patients were provided DASH meals in a controlled environment.[7,8] A subsequent randomized trial to examine the efficacy of the DASH diet in an outpatient setting, the PREMIER Study,[9] demonstrated that the DASH diet could be successfully implemented in free-living persons. Both "established" JNC 6[10] recommendations and the JNC 6 recommendations plus the DASH diet (ie, JNC 7 recommendations[6]) were associated with significant BP reductions compared with advice-only controls. In an ancillary study, Ard et al[11] reported results
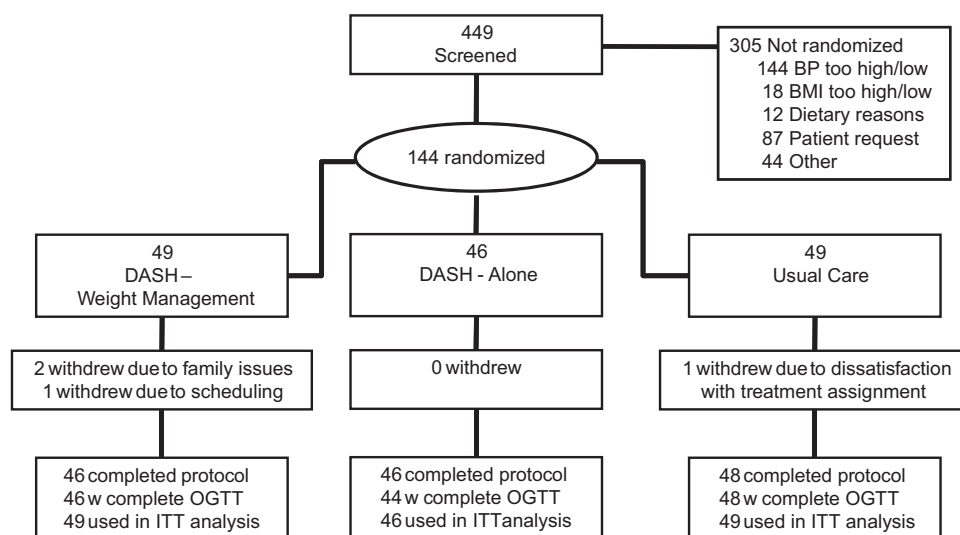
Figure 1. Participant flow in the ENCORE clinical trial. ITT refers to intent to treat.

from a subsample of 52 PREMIER participants who received an oral glucose tolerance test (OGTT) at baseline and after 6 months of treatment. Those who received the established intervention with or without the DASH diet showed greater improvements in fasting insulin and glucose compared with controls, but only the "established-plus-DASH" intervention achieved greater improvements in insulin sensitivity. However, because participants in the established-plus-DASH treatment tended to lose more weight and reduce their waist circumference compared with participants in both the advice-only control condition and the JNC 6 established intervention condition, the incremental benefit of the DASH diet to lifestyle modifications of weight loss, exercise, and sodium restriction could not be determined.

In an effort to examine the independent and combined effects of the DASH diet and weight loss plus exercise on BP and biomarkers of risk, the Exercise and Nutritional Interventions for Cardiovascular Health (ENCORE) Study examined 4 months of treatment with the DASH diet alone, without exercise or weight loss (DASH-A), or the DASH diet combined with a behavioral weight management program, including caloric restriction and aerobic exercise (DASH-WM), in 144 men and women with HBP.[12] Results showed that both DASH-A and DASH-WM were associated with larger BP reductions compared with a usual diet control (UC) group, although the DASH-WM condition achieved larger BP reductions and greater improvements in such cardiovascular biomarkers as pulse wave velocity, baroreflex sensitivity, and left ventricular mass. The present study reports the findings from the ENCORE Study on the secondary outcomes of insulin sensitivity and lipids.

Methods

Participants

As described in our primary article,[12] the ENCORE Trial enrolled 144 healthy but overweight adults with HBP (Figure 1). Persons were eligible if they were not taking antihypertensive medication and had a mean systolic BP of 130 to 159 mm Hg or diastolic BP 85 to 99 mm Hg averaged over 4 separate BP screening visits. Potential participants were asked to refrain from smoking or ingesting caffeine for $\geq$30 minutes before their appointment time. BP measurements were standardized for cuff size, position, environment, and time of

day. Other inclusion criteria included age $\geq$35 years, body mass index (BMI) of 25 to 40 kg/m^2, sedentary lifestyle (ie, not engaged in regular exercise), and no other medical comorbidities that would preclude safe participation in the trial, including diabetes mellitus requiring insulin or oral hypoglycemic agents. Clinic BPs were determined according to JNC 7 guidelines using a standard mercury sphygmomanometer and stethoscope.

Trial Overview

The ENCORE Study was approved by the institutional review board at Duke University Medical Center, and written informed consent was obtained from all of the participants. After completion of a series of baseline assessments (see below), participants were randomized to DASH-A, DASH-WM, or UC. At the conclusion of the 4-month treatment period, assessments were repeated.

Assessments of Body Composition, Dietary Content, and Aerobic Fitness

Body weight was measured by a standard balance scale with participants dressed in light clothing without shoes. Body composition and fat distribution were assessed by dual energy absorptiometry. This procedure provides measurements of fat mass, lean body mass, and percentage of body fat for both the whole body and designated anatomic subregions.[13] An independent assessment of dietary and nutritional content was obtained by 2 separate self-report measures of diet: a retrospective food frequency questionnaire,[14] requiring participants to recall typical consumption over a 4-week period, and a 4-day food diary. The food frequency questionnaire was analyzed by NutritionQuest, whereas the diary data were analyzed using Food Processor SQL Edition software (version 10.3, ESHA Research).[15] Fitness was measured with a maximal graded exercise treadmill test in which workloads were increased at a rate of 1 metabolic equivalent per minute.[16] Expired air was collected by mouthpiece for quantification of minute ventilation, oxygen consumption, and carbon dioxide production with a Parvo Medics True One measurement system (model 2400; Parvo Medics).

Assessments of Insulin Sensitivity and Lipids

Measures of glucose tolerance and insulin sensitivity were based on results of an OGTT using an oral glucose load of 75 g, with measurement of plasma glucose (by Beckman auto-analyzer) at 0, 30, 60, 90, and 120 minutes and insulin (by double-antibody radioimmunoassay) at 0 and 120 minutes. Insulin sensitivity was assessed using the quantitative insulin sensitivity check index, as described by Katz et al,[17] and using a method based on dynamic glucose and insulin levels, the insulin sensitivity index, as described

by Gutt et al.[18] Both of these surrogate measures of insulin sensitivity provide estimates of insulin sensitivity that correlate closely with glucose clamp measurements and are predictive of the onset of type 2 diabetes mellitus.[19,20]

Lipid profiles, including total cholesterol, high-density lipoprotein, low-density lipoprotein (LDL) cholesterol, very LDL cholesterol, and triglycerides, were obtained from fasting blood samples drawn between 8:00 and 9:00 AM. Assays were measured enzymatically (Labcorp Inc).

Randomization

On completion of the baseline assessments, patients were randomized in blocks of 2 to 5 participants. Participants were provided their group assignments in sealed envelopes; staff members performing assessments were unaware of participant treatment group assignments. Assignments were stratified by baseline clinic BP, BMI, and age.

Interventions

Immediately after randomization, participants received 2-week controlled feeding on the Duke Clinical Research Unit, in which they ate the assigned dietary patterns (controlled usual diet, DASH diet, or a reduced-calorie DASH diet). Participants ate their evening meal on the unit and took home their breakfast, lunch, and snack for the following day. The controlled feeding period was modeled after the original DASH feeding studies.[7,8] Participants in the DASH-A and UC conditions consumed study meals isocalorically for weight maintenance, whereas the caloric level in the DASH-WM arm was set at a 500-calories-per-day deficit to allow weight loss of ≈0.5 to 1.0 pound a week.

After the first 2 weeks of controlled feeding, participants were instructed to maintain the DASH-WM or the DASH-A diet. Participants in the DASH-A condition met weekly with a nutritionist and modified the content of their diet to meet DASH guidelines but did not exercise or attempt to lose weight.

Participants in the DASH-WM condition received the same instruction in the DASH diet from the same nutritionist as in the DASH-A group but also met with a clinical health psychologist who provided a structured, cognitive behavioral weight loss intervention that used cognitive behavioral strategies[21] and appetite awareness training.[22] The DASH recommendations provided participants with guidance regarding what to eat, whereas weight management was designed to help individuals learn when, how, and how much to eat. Participants also engaged in supervised exercise 3 times per week for 30 minutes at a level of 70% to 85% of their initial heart rate reserve determined during their baseline treadmill test.

Participants in the UC condition were asked to maintain their usual dietary and exercise habits for 4 months until they were re-evaluated. Weight and BP were monitored biweekly.

Statistical Analysis

Treatment effects were evaluated using the general linear model in the SAS 9.1 software (SAS Institute), with separate models for each outcome. Each model included treatment condition as a 3-level factor and the corresponding pretreatment value of the outcome, age, sex, and ethnicity (white versus nonwhite) as adjustment covariables. We compared posttreatment group means using pairwise treatment group comparisons that were adjusted using the Tukey honestly significant difference procedure. Data for all of the outcomes were analyzed after the intent-to-treat principle, with missing data managed using the multiple imputation method available in SAS PROC MI. For a given outcome, we estimated that we would have ≈80% power to detect a 0.5 SD difference between the active treatments and UC and a 0.6 SD difference between DASH-A and DASH-WM.

Results

Participant Flow

As described previously,[12] 3129 participants initially inquired about the study, 449 met our initial inclusion criteria, and 144

Table 1. Background Characteristics of the Sample

Demographics	DASH-WM (n=49)	DASH-A (n=46)	UC (n=49)	All (n=144)
Age, y	52.3 (10)	51.8 (10)	51.8 (9)	52.0 (10)
Sex, female, % (n)	69 (34)	63 (29)	69 (34)	67 (97)
Ethnicity, % (n)				
White	69 (34)	50 (23)	59 (29)	60 (86)
Black	31 (15)	48 (22)	39 (19)	39 (56)
Asian	0 (0)	2 (1)	2 (1)	1 (2)
Level of education, % (n)				
High school	31 (15)	30 (14)	42 (20)	34 (49)
Some college	8 (4)	9 (4)	14 (7)	11 (15)
Completed college	29 (14)	30 (14)	18 (9)	22 (32)
Postgraduate school	20 (10)	28 (13)	20 (10)	24 (34)
Other	12 (6)	13 (6)	2 (1)	9 (13)
Weight, kg	93.9 (14)	93.0 (14)	92.6 (15)	93.1 (14.1)
BMI, kg/m^2	33.5 (4.4)	32.8 (3.4)	33.0 (3.9)	33.1 (3.9)

Values are mean (SD) for continuous variables and group percent (n) for categories.

participants were randomized to the DASH-WM (n=49), DASH-A (n=46), or UC (n=49) diet. Posttreatment glucose and lipid data were available for 46 participants in DASH-WM, 44 in DASH-A, and 48 in the UC group. For body composition variables, posttreatment data were available for 46 participants in DASH-WM, 46 in DASH-A, and 47 in the UC group.

Participant Characteristics

Table 1 displays the demographic and medical characteristics of the sample across the 3 treatment groups at baseline. On average, participants were 52 years old; 39% were black and 67% were women. The mean clinic BP was 138/86 mm Hg. The majority of participants were college educated and relatively affluent. The groups were generally comparable across the background variables.

Adherence to Protocol

Attendance to the exercise and diet classes was excellent. DASH-WM participants attended 90% (median: 38) of scheduled exercise sessions and spent most time (median: 94%) at or above their target heart rate training range. DASH dietary class attendance also was excellent, with the median number of sessions attended at 12 (92%) in both intervention groups. As reported previously,[12] compared with DASH-A and UC, participants in DASH-WM on average consumed significantly fewer total calories (1648 kcal [95% CI: 1521 to 1774 kcal], 1962 kcal [95% CI: 1833 to 2090 kcal], and 2095 kcal [95% CI: 1961 to 2228 kcal] for DASH-WM, DASH-A, and UC, respectively), and both DASH conditions consumed more calories from protein (19.5%, 19.4%, and 16.7% for DASH-WM, DASH-A, and UC, respectively), less saturated fat (26.3%, 27.8%, and 36.8% for DASH-WM, DASH-A, and UC, respectively), and more fiber (25, 26, and 16 g for DASH-WM, DASH-A, and UC, respectively) compared with those in UC (P<0.001).

Changes in Body Weight and Body Composition

Adjusting for baseline weight, age, sex, and ethnicity, the mean posttreatment weight for the DASH-WM group was

Table 2. **Body Composition (Dual Energy Absorptiometry) Measures Before and After Treatment**

Variable	Time	Treatment Group, DASH-WM	DASH-A	UC	P Value From Pairwise Comparison After Treatment		
					DASH-WM vs DASH-A	DASH-WM vs UC	DASH-A vs UC
Total percentage of body fat	Before	37.6 (35.5 to 39.7)	35.4 (33.2 to 37.5)	36.4 (34.3 to 38.5)			
	After	33.1 (32.4 to 33.8)	36.2 (35.5 to 36.8)	36.9 (36.2 to 37.6)	<0.001	<0.001	0.293
Total lean body mass, kg	Before	56.0 (53.0 to 59.1)	57.5 (54.2 to 60.7)	56.7 (53.7 to 59.8)			
	After	54.3 (53.8 to 54.9)	56.8 (56.2 to 57.4)	56.5 (55.9 to 57.0)	<0.001	<0.001	0.694
Total trunk fat, kg	Before	17.7 (16.4 to 19.0)	16.2 (14.9 to 17.5)	16.9 (15.6 to 18.2)			
	After	13.6 (13.1 to 14.1)	16.6 (16.1 to 17.1)	17.1 (16.7 to 17.6)	<0.001	<0.001	0.217

Values are mean and 95% CI. Values after treatment are adjusted for pretreatment levels of outcome variable, age, sex, and ethnicity. P values are adjusted using the Tukey honestly significant difference procedure.

significantly lower (84.5 kg) compared with DASH-A (92.9 kg; $P<0.001$) and UC (94.1 kg; $P<0.001$). The weight change was -8.7 kg in DASH-WM, -0.3 kg in DASH-A, and $+0.9$ kg in UC.

After treatment, the DASH-WM group showed a lower percentage of body fat and trunk fat compared with the DASH-A and UC groups (Table 2). DASH-WM also had lower lean body mass compared with the other groups. DASH-A did not differ significantly from UC on any body composition measure.

Changes in Aerobic Fitness

Adjusting for pretreatment levels, age, sex, and ethnicity, the mean posttreatment peak maximal oxygen consumption was higher in DASH-WM (29 mL/kg per minute) compared with DASH-A (23 mL/kg per minute; $P<0.001$) and UC (22 mL/kg per minute; $P<0.001$). Participants in the DASH-WM group showed a 19% increase in peak maximal oxygen consumption compared with small and nonsignificant decreases in the DASH-A (-1.2%) and UC (-3.2%) groups.

Glucose Tolerance and Insulin Sensitivity

Results of the OGTT revealed that participants in the DASH-WM condition achieved greater improvements in glucose response compared with DASH-A and UC (Figure 2). Compared with UC, participants in the DASH-WM group showed lower fasting glucose levels (Table 3). DASH-WM also

exhibited lower glucose area under the curve and greater insulin sensitivity, as measured by both quantitative insulin sensitivity check index and insulin sensitivity index compared with the DASH-A or UC group. DASH-A did not differ from UC on any measure of glucose metabolism or insulin sensitivity.

We also noted that 24% (n=34) of participants were considered overweight (BMI: 25 to 29.9), whereas 76% (n=110) were considered obese (BMI: >30) at baseline. The treatment group by BMI interaction was not significant, however, for glucose area under the curve ($P=0.385$), quantitative insulin sensitivity check index ($P=0.528$), or insulin sensitivity index ($P=0.142$), suggesting that pretreatment body weight did not moderate the effects of treatment on glucose metabolism or insulin sensitivity.

In a post hoc analysis, participants were classified as diabetic (>199 mg/dL), prediabetic (141 to 199 mg/dL), or normal (<140 mg/dL) on the basis of their glucose levels at 2 hours during the OGTT. Overall, 72% (n=13) of the 18 participants in DASH-WM who were either prediabetic or diabetic at study entry improved by ≥1 category over the course of the trial, compared with 54% (7 of 13) in DASH-A and 42% (8 of 19) in the UC group. Among participants who were either not diabetic or prediabetic on study entry, diabetic classification worsened in only 2% (1 of 44) of participants in DASH-WM compared with 16% (7 of 43) in DASH-A and 11% (5 of 46) in the UC group.

Serum Lipids

Participants in the DASH-WM group obtained significantly lower total cholesterol and triglyceride levels compared with DASH-A and UC participants and lower LDL cholesterol levels compared with UC but not DASH-A (Table 4). Participants in DASH-A had marginally lower high-density lipoprotein cholesterol levels than UC, but otherwise participants in DASH-A were not different from UC participants on any other lipid measure.

Discussion

Our findings demonstrate that adherence to the DASH diet alone, although sufficient to modify BP values,[12] resulted in significant improvements in metabolic indices of cardiovascular risk only when accompanied by aerobic exercise and weight loss. In the DASH-WM group, participants lost an average of 19 pounds over 4 months and increased their aerobic capacity by 19%. Although both the DASH-A and
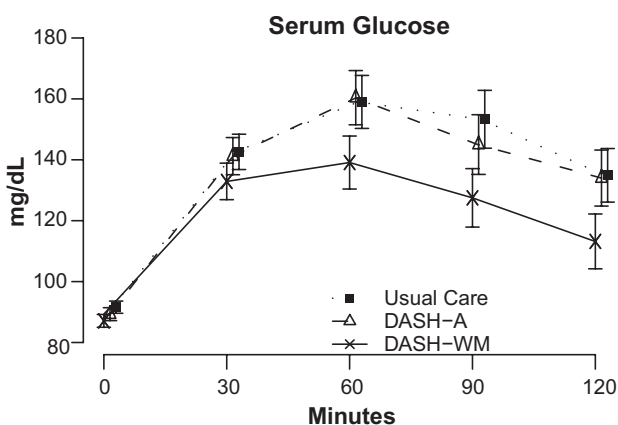

Figure 2. Posttreatment glucose response during OGTT. Values are adjusted for pretreatment glucose levels, sex, age, and ethnicity. Error bars represent 95% confidence limits.

Table 3. Glucose and Insulin Values Before and After Treatment

Variable	Time	Treatment Group			P Value From Pairwise Comparison After Treatment		
		DASH-WM	DASH-A	UC	DASH-WM vs DASH-A	DASH-WM vs UC	DASH-A vs UC
Fasting glucose, mg/dL	Before	89.4 (86.4 to 92.3)	90.4 (87.3 to 93.5)	91.3 (88.4 to 94.3)			
	After	87.2 (85.1 to 89.3)	89.4 (87.3 to 91.5)	91.9 (89.9 to 93.9)	0.324	0.006	0.214
Fasting insulin, μU/mL	Before	18.1 (15.7 to 20.4)	16.6 (14.2 to 19.0)	18.0 (15.7 to 20.3)			
	After	12.5 (10.8 to 14.3)	17.6 (15.9 to 19.4)	18.6 (16.9 to 20.2)	<0.001	<0.001	0.711
Glucose AUC, mg/dL · min	Before	6057 (5221 to 6893)	6087 (5224 to 6951)	6345 (5508 to 7181)			
	After	4947 (4340 to 5554)	6238 (5637 to 6838)	6334 (5756 to 6912)	0.011	0.005	0.958
$ISI_{0,120}$, mg · L^2/ mmol · μU · min	Before	74.4 (67.1 to 81.8)	70.9 (63.5 to 78.3)	66.0 (58.8 to 73.2)			
	After	75.3 (71.8 to 78.8)	68.7 (65.1 to 72.3)	68.8 (65.4 to 72.2)	0.031	0.026	0.981
QUICKI	Before	0.319 (0.313 to 0.325)	0.319 (0.313 to 0.325)	0.315 (0.309 to 0.321)			
	After	0.334 (0.329 to 0.339)	0.318 (0.313 to 0.323)	0.316 (0.312 to 0.321)	<0.001	<0.001	0.850

Values are mean and 95% CI. Values after treatment are adjusted for pretreatment levels of outcome variable, age, sex, and ethnicity. P values are adjusted using the Tukey honestly significant difference procedure. QUICKI indicates quantitative insulin sensitivity check index; $ISI_{0, 120}$, insulin sensitivity index; AUC, area under the curve.

DASH-WM groups achieved clinically meaningful reductions in BP and improvements in other cardiovascular biomarkers of risk, as described in our earlier publication,[12] only DASH-WM participants demonstrated significant improvements in glucose tolerance and insulin sensitivity.

Although the DASH diet has been shown to reduce BP in controlled feeding studies[7,8] and in studies of free-living individuals,[9,12] the present study found that ENCORE participants who adhered to the DASH diet but did not exercise or lose weight achieved minimal improvements in glucose metabolism, insulin sensitivity, and lipids, relative to controls. Our findings contrast with results from the PREMIER substudy,[11] in which the addition of the DASH diet to an established intervention of weight loss, reduced sodium intake, increased physical activity, and moderation of alcohol intake resulted in a significant improvement in insulin sensitivity relative to controls. However, because there was no difference in insulin sensitivity between groups randomized to the established intervention with or without the DASH diet and there was a trend toward greater weight loss in the DASH group, the added value of the DASH diet is uncertain. The present ENCORE Study findings indicate that, despite DASH-related reductions in BP,[12] the DASH diet by itself produced minimal improvements in insulin sensitivity.

Our study was designed to evaluate only the DASH diet, and it is possible, even likely, that other diets, either alone or combined with exercise, could be beneficial. Many studies have examined the impact of various diets on weight loss.[23–26] Sacks et al,[23] for example, randomized overweight adults to 1 of 4 diets in which the targeted percentages of energy derived from fat, protein, and carbohydrates varied. After 2 years, groups achieved similar benefits in weight loss and lipid-related risk factors and fasting insulin levels. It was concluded that reduced-calorie diets result in significant weight loss regardless of the macronutrient content. Foster et al[25] reported that a low-carbohydrate, high-protein, and high-fat (Atkins) diet was associated with greater weight loss after 6 months compared with a conventional low fat, low-calorie, high-carbohydrate diet but that the differences were not significant after 12 months. With respect to body composition, the present findings confirm the results of previous findings suggesting that a low-fat weight loss diet (50% carbohydrate, 30% fat, and 20% protein) results in reduced lean body mass. However, very low-carbohydrate diets have been found to result in even greater reductions in weight and lean body mass compared with low-fat diets.[27–29] Lipid changes were generally similar over time, and both diets were

Table 4. Serum Lipids Before and After Treatment

Variable	Time	Treatment Group			P Value From Pairwise Comparison After Treatment		
		DASH-WM	DASH-A	UC	DASH-WM vs DASH-A	DASH-WM vs UC	DASH-A vs UC
Total cholesterol, mg/dL	Before	209 (198 to 220)	199 (188 to 211)	206 (195 to 217)			
	After	184 (177 to 199)	199 (192 to 205)	205 (199 to 211)	0.008	<0.001	0.364
LDL cholesterol, mg/dL	Before	128 (118 to 138)	122 (112 to 132)	126 (116 to 136)			
	After	112 (106 to 117)	122 (116 to 127)	125 (119 to 130)	0.054	0.005	0.715
High density lipoprotein cholesterol, mg/dL	Before	55 (50 to 59)	53 (49 to 57)	55 (51 to 59)			
	After	54 (52 to 55)	51 (50 to 53)	54 (53 to 56)	0.115	0.911	0.047
Triglycerides, mg/dL	Before	133 (116 to 149)	122 (106 to 139)	122 (106 to 139)			
	After	93 (81 to 106)	129 (117 to 142)	130 (118 to 142)	<0.001	<0.001	0.900

Values are mean and 95% CI. Values after treatment are adjusted for pretreatment levels of outcome variable, age, sex, and ethnicity. P values are adjusted using the Tukey honestly significant difference procedure.

associated with lower diastolic BP and insulin response to an oral glucose load.

Although weight loss is associated with improved lipids, particularly LDL cholesterol,[30] and increased insulin sensitivity,[31–33] diet composition may also affect lipids and glucose metabolism independent of weight loss. For example, with a 4-week, isocaloric weight maintenance diet, both the Ornish diet and South Beach diet have been shown to favorably reduce lipids, whereas high-fat diets may be associated with increased LDL and total cholesterol levels.[34] However, the number of calories consumed appears to be more important relative to the content of the calories with regard to the development of diabetes mellitus.[35]

Exercise also was a key component of the DASH-WM intervention, but its effects on insulin sensitivity could not be determined independent from weight loss. Although exercise is widely considered to be important for successful weight loss, studies of the effects of exercise in the absence of weight loss on glucose, insulin sensitivity, and lipids have produced mixed results. Exercise has been shown to improve insulin sensitivity, either because of chronic effects of exercise training or the residual effects of acute exercise. Studies of both healthy adults and patients with type 2 diabetes mellitus have demonstrated that improved insulin sensitivity is maintained ≤16 hours after a single bout of exercise[36,37] but may be diminished 60 hours after the final exercise training session.[38,39] Some studies have demonstrated that exercise training is associated with reduced glucose levels and improved glycemic control,[40–44] whereas others have not.[45–50] Because studies that have shown improvements in glucose control after exercise training have not established that these effects are attributed to exercise independent of weight loss,[51] the extent to which the exercise component of the DASH-WM condition contributed to the metabolic improvements observed in the ENCORE Study is not known. The effects of exercise training on lipids also have provided mixed results,[52] although recent evidence suggests that high levels of exercise without weight loss may be required to achieve improvements in lipid and lipoprotein variables.[53]

Finally, it should be noted that some studies have also suggested that obesity may moderate the effects of exercise training on insulin sensitivity. Poirier et al,[48] for example, reported no improvement in insulin sensitivity in obese type 2 diabetic patients after 12 weeks of aerobic training, although insulin sensitivity was improved in nonobese type 2 diabetic subgroups. Our data in overweight but nondiabetic patients revealed no evidence that obesity moderated the effects of treatment. Therefore, our findings suggest that the improvements in insulin sensitivity observed in the DASH-WM intervention are generalizable to both obese and nonobese populations.

Perspectives

In summary, the results of the ENCORE Study indicate that, whereas the DASH diet alone can reduce BP in overweight, sedentary adults with HBP, there was little evidence that the DASH diet improved insulin sensitivity or lipids without the addition of exercise and weight reduction. It would appear that caloric consumption rather than nutrient composition is most salient for improved metabolic function.

Disclosures

None.

References

1. Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999–2004. *Hypertension*. 2007;49:69–75.
2. Neal B, MacMahon S, Chapman N, Blood Pressure Lowering Treatment Trialists C. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials: Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2000;356:1955–1964.
3. Adverse reactions to bendrofluazide and propranolol for the treatment of mild hypertension: report of Medical Research Council Working Party on Mild to Moderate Hypertension. *Lancet*. 1981;2:539–543.
4. Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *BMJ*. 2003;326:1427.
5. Elliott WJ, Meyer PM. Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis. *Lancet*. 2007;369:201–207.
6. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ, for the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206–1252.
7. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure: DASH Collaborative Research Group. *N Engl J Med*. 1997;336:1117–1124.
8. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER III, Simons-Morton DG, Karanja N, Lin PH, Group DA-SCR. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet: DASH-Sodium Collaborative Research Group. *N Engl J Med*. 2001; 344:3–10.
9. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, Stevens VJ, Vollmer WM, Lin PH, Svetkey LP, Stedman SW, Young DR, Writing Group of the PCRG. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA*. 2003;289:2083–2093.
10. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med*. 1997;157:2413–2446.
11. Ard JD, Grambow SC, Liu D, Slentz CA, Kraus WE, Svetkey LP. The effect of the PREMIER interventions on insulin sensitivity. *Diabetes Care*. 2004;27:340–347.
12. Blumenthal JA, Babyak MA, Hinderliter A, Watkins LL, Craighead L, Lin P-H, Caccia C, Johnson J, Waugh RA, Sherwood A. Effects of the DASH diet alone and in combination with exercise and weight loss on blood pressure and cardiovascular biomarkers in men and women with high blood pressure: the ENCORE Study. *Arch Intern Med*. 2010;170: 126–135.
13. Treuth MS, Hunter GR, Kekes-Szabo T. Estimating intraabdominal adipose tissue in women by dual-energy X-ray absorptiometry. *Am J Clin Nutr*. 1995;62:527–532.
14. Eck LH, Klesges RC, Hanson CL, Slawson D, Portis L, Lavasque ME. Measuring short-term dietary intake: development and testing of a 1-week food frequency questionnaire. *J Am Diet Assoc*. 1991;91:940–945.

15. Bazzano LA, He J, Ogden LG, Loria CM, Vupputuri S, Myers L, Whelton PK. Agreement on nutrient intake between the databases of the First National Health and Nutrition Examination Survey and the ESHA Food Processor. *Am J Epidemiol*. 2002;156:78–85.

16. Blumenthal JA, Emery CF, Rejeski WJ. The effects of exercise training on psychosocial functioning after myocardial infarction. *J Cardpulm Rehabil*. 1988;8:183–193.

17. Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, Quon MJ. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab*. 2000;85:2402–2410.

18. Gutt M, Davis CL, Spitzer SB, Llabre MM, Kumar M, Czarnecki EM, Schneiderman N, Skyler JS, Marks JB. Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. *Diabetes Res Clin Pract*. 2000;47:177–184.

19. Hanley AJ, Williams K, Gonzalez C, D'Agostino RB Jr, Wagenknecht LE, Stern MP, Haffner SM. Prediction of type 2 diabetes using simple measures of insulin resistance: combined results from the San Antonio Heart Study, the Mexico City Diabetes Study, and the Insulin Resistance Atherosclerosis Study. *Diabetes*. 2003;52:463–469.

20. Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin sensitivity and resistance in vivo: advantages, limitations, and appropriate usage. *Am J Physiol Endocrinol Metab*. 2008; 294:E15–E26.

21. Fairburn CG. *Cognitive-Behavioral Treatment of Obesity: A Clinican's Guide*. New York, NY: Guilford Press; 2003.

22. Craighead L. *The Appetite Awareness Workbook: How to Listen to Your Body and Overcome Binge Eating, Overeating, and Obsession With Food*. Oakland, CA: New Harbinger; 2006.

23. Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, McManus K, Champagne CM, Bishop LM, Laranjo N, Leboff MS, Rood JC, de Jonge L, Greenway FL, Loria CM, Obarzanek E, Williamson DA. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med*. 2009;360:859–873.

24. Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, Golan R, Fraser D, Bolotin A, Vardi H, Tangi-Rozental O, Zuk-Ramot R, Sarusi B, Brickner D, Schwartz Z, Sheiner E, Marko R, Katorza E, Thiery J, Fiedler GM, Bluher M, Stumvoll M, Stampfer MJ. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med*. 2008; 359:229–241.

25. Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed BS, Szapary PO, Rader DJ, Edman JS, Klein S. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med*. 2003;348:2082–2090.

26. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS Jr, Brehm BJ, Bucher HC. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Arch Intern Med*. 2006;166:285–293.

27. Noakes M, Foster P, Keogh J, James A, Mamo J, Clifton P. Comparison of isocaloric very low carbohydrate/high saturated fat and high carbohydrate/low saturated fat diets on body composition and cardiovascular risk. *Nutr Metab*. 2006;3:7.

28. Meckling KA, O'Sullivan C, Saari D. Comparison of a low-fat diet to a low-carbohydrate diet on weight loss, body composition, and risk factors for diabetes and cardiovascular disease in free-living, overweight men and women. *J Clin Endocrinol Metab*. 2004;89:2717–2723.

29. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *J Clin Endocrinol Metab*. 2003;88:1617–1623.

30. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *Am J Clin Nutr*. 1992;56: 320–328.

31. Goodpaster BH, Kelley DE, Wing RR, Meier A, Thaete FL. Effects of weight loss on regional fat distribution and insulin sensitivity in obesity. *Diabetes*. 1999;48:839–847.

32. Rice B, Janssen I, Hudson R, Ross R. Effects of aerobic or resistance exercise and/or diet on glucose tolerance and plasma insulin levels in obese men. *Diabetes Care*. 1999;22:684–691.

33. Dengel DR, Pratley RE, Hagberg JM, Rogus EM, Goldberg AP. Distinct effects of aerobic exercise training and weight loss on glucose homeostasis in obese sedentary men. *J Appl Physiol*. 1996;81:318–325.

34. Miller M, Beach V, Sorkin JD, Mangano C, Dobmeier C, Novacic D, Rhyne J, Vogel RA. Comparative effects of three popular diets on lipids,

endothelial function, and C-reactive protein during weight maintenance. *J Am Diet Assoc*. 2009;109:713–717.

35. Feinglos MN, Totten SE. Are you what you eat, or how much you eat? The case of type 2 diabetes mellitus. *Arch Intern Med*. 2008;168: 1485–1486.

36. Mikines KJ, Sonne B, Tronier B, Galbo H. Effects of training and detraining on dose-response relationship between glucose and insulin secretion. *Am J Physiol*. 1989;256:E588–E596.

37. Devlin JT, Hirshman M, Horton ED, Horton ES. Enhanced peripheral and splanchnic insulin sensitivity in NIDDM men after single bout of exercise. *Diabetes*. 1987;36:434–439.

38. Burstein R, Polychronakos C, Toews CJ, MacDougall JD, Guyda HJ, Posner BI. Acute reversal of the enhanced insulin action in trained athletes. Association with insulin receptor changes. *Diabetes*. 1985;34: 756–760.

39. Giacca A, Groenewoud Y, Tsui E, McClean P, Zinman B. Glucose production, utilization, and cycling in response to moderate exercise in obese subjects with type 2 diabetes and mild hyperglycemia. *Diabetes*. 1998;47:1763–1770.

40. Barnard RJ, Jung T, Inkeles SB. Diet and exercise in the treatment of NIDDM: the need for early emphasis. *Diabetes Care*. 1994;17: 1469–1472.

41. Yamanouchi K, Shinozaki T, Chikada K, Nishikawa T, Ito K, Shimizu S, Ozawa N, Suzuki Y, Maeno H, Kato K. Daily walking combined with diet therapy is a useful means for obese NIDDM patients not only to reduce body weight but also to improve insulin sensitivity. *Diabetes Care*. 1995;18:775–778.

42. Schneider SH, Khachadurian AK, Amorosa LF, Clemow L, Ruderman NB. Ten-year experience with an exercise-based outpatient life-style modification program in the treatment of diabetes mellitus. *Diabetes Care*. 1992;15:1800–1810.

43. Vanninen E, Uusitupa M, Siitonen O, Laitinen J, Lansimies E. Habitual physical activity, aerobic capacity and metabolic control in patients with newly-diagnosed type 2 (non-insulin-dependent) diabetes mellitus: effect of 1-year diet and exercise intervention. *Diabetologia*. 1992;35:340–346.

44. Trovati M, Carta Q, Cavalot F, Vitali S, Banaudi C, Lucchina PG, Fiocchi F, Emanuelli G, Lenti G. Influence of physical training on blood glucose control, glucose tolerance, insulin secretion, and insulin action in non-insulin-dependent diabetic patients. *Diabetes Care*. 1984;7:416–420.

45. Skarfors ET, Wegener TA, Lithell H, Selinus I. Physical training as treatment for type 2 (non-insulin-dependent) diabetes in elderly men: a feasibility study over 2 years. *Diabetologia*. 1987;30:930–933.

46. Bogardus C, Lillioja S, Howard BV, Reaven G, Mott D. Relationships between insulin secretion, insulin action, and fasting plasma glucose concentration in nondiabetic and noninsulin-dependent diabetic subjects. *J Clin Invest*. 1984;74:1238–1246.

47. Cauza E, Hanusch-Enserer U, Strasser B, Ludvik B, Metz-Schimmerl S, Pacini G, Wagner O, Georg P, Prager R, Kostner K, Dunky A, Haber P. The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. *Arch Phys Med Rehabil*. 2005;86:1527–1533.

48. Poirier P, Tremblay A, Broderick T, Catellier C, Tancrede G, Nadeau A. Impact of moderate aerobic exercise training on insulin sensitivity in type 2 diabetic men treated with oral hypoglycemic agents: is insulin sensitivity enhanced only in nonobese subjects? *Med Sci Monit*. 2002;8: CR59–CR65.

49. Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD, Frohlich JJ. Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. *Diabetes Care*. 2003;26:2977–2982.

50. Blumenthal JA, Sherwood A, Gullette ECD, Babyak M, Waugh RH, Georgiades A, Craighead LW, Tweedy D, Feinglos M, Appelbaum M, Hayano J, Hinderliter A. Exercise and weight loss reduce blood pressure in men and women with mild hypertension. *Arch Intern Med*. 2000;160: 1942–1958.

51. Feuerstein BL, Weinstock RS. Diet and exercise in type 2 diabetes mellitus. *Nutrition*. 1997;13:95–99.

52. Leon AS, Sanchez OA. Response of blood lipids to exercise training alone or combined with dietary intervention. *Med Sci Sports Exerc*. 2001;33:S502–S515.

53. Kraus WE, Houmard JA, Duscha BD, Knetzger KJ, Wharton MB, McCartney JS, Bales CW, Henes S, Samsa GP, Otvos JD, Kulkarni KR, Slentz CA. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med*. 2002;347:1483–1492.

Hypertension

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Effects of the Dietary Approaches to Stop Hypertension Diet Alone and in Combination With Exercise and Caloric Restriction on Insulin Sensitivity and Lipids
James A. Blumenthal, Michael A. Babyak, Andrew Sherwood, Linda Craighead, Pao-Hwa Lin, Julie Johnson, Lana L. Watkins, Jenny T. Wang, Cynthia Kuhn, Mark Feinglos and Alan Hinderliter

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/55/5/1199