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

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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. 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 610 recommendations and the JNC 6 recommendations plus the DASH diet (ie, JNC 7 recommendations8) were associated with significant BP reductions compared with advice-only controls. In an ancillary study, Ard et al11 reported results...
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. 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, 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 ≥30 minutes before their appointment time. BP measurements were standardized for cuff size, position, environment, and time of day. Other inclusion criteria included age ≥35 years, body mass index (BMI) of 25 to 40 kg/m², 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. An independent assessment of dietary and nutritional content was obtained by 2 separate self-report measures of diet: a retrospective food frequency questionnaire, 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). Fitness was measured with a maximal graded exercise treadmill test in which workloads were increased at a rate of 1 metabolic equivalent per minute. 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, 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 per 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 strategies21 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 covariates. 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 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>
<thead>
<tr>
<th>Demographics</th>
<th>DASH-WM (n=49)</th>
<th>DASH-A (n=46)</th>
<th>UC (n=49)</th>
<th>All (n=144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>52.3 (10)</td>
<td>51.8 (10)</td>
<td>51.8 (9)</td>
<td>52.0 (10)</td>
</tr>
<tr>
<td>Sex, female, % (n)</td>
<td>69 (34)</td>
<td>63 (29)</td>
<td>69 (34)</td>
<td>67 (97)</td>
</tr>
<tr>
<td>Ethnicity, % (n)</td>
<td>69 (34)</td>
<td>50 (23)</td>
<td>59 (29)</td>
<td>60 (86)</td>
</tr>
<tr>
<td>White</td>
<td>31 (15)</td>
<td>48 (22)</td>
<td>39 (19)</td>
<td>39 (56)</td>
</tr>
<tr>
<td>Black</td>
<td>0 (0)</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Asian</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Level of education, % (n)</td>
<td>31 (15)</td>
<td>30 (14)</td>
<td>42 (20)</td>
<td>34 (49)</td>
</tr>
<tr>
<td>High school</td>
<td>8 (4)</td>
<td>9 (4)</td>
<td>14 (7)</td>
<td>11 (15)</td>
</tr>
<tr>
<td>Some college</td>
<td>29 (14)</td>
<td>30 (14)</td>
<td>18 (9)</td>
<td>22 (32)</td>
</tr>
<tr>
<td>Completed college</td>
<td>20 (10)</td>
<td>28 (13)</td>
<td>20 (10)</td>
<td>24 (34)</td>
</tr>
<tr>
<td>Postgraduate school</td>
<td>12 (6)</td>
<td>13 (6)</td>
<td>2 (1)</td>
<td>9 (13)</td>
</tr>
<tr>
<td>Other</td>
<td>93.9 (14)</td>
<td>93.0 (14)</td>
<td>92.6 (15)</td>
<td>93.1 (14.1)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>33.5 (4.4)</td>
<td>32.8 (3.4)</td>
<td>33.0 (3.9)</td>
<td>33.1 (3.9)</td>
</tr>
</tbody>
</table>

Values are mean (SD) for continuous variables and group percent (% n) for categories.
Our findings demonstrate that adherence to the DASH diet alone, although sufficient to modify BP values, 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
DASH-WM groups achieved clinically meaningful reductions in BP and improvements in other cardiovascular biomarkers of risk, as described in our earlier publication, 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 and in studies of free-living individuals, 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, 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, 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. Sacks et al, 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 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.

DASH-A vs UC

Table 3. Glucose and Insulin Values Before and After Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Treatment Group</th>
<th>P Value From Pairwise Comparison After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>Before</td>
<td>89.4 (86.4 to 92.3)</td>
<td>90.4 (87.3 to 93.5)</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>87.2 (85.1 to 89.3)</td>
<td>89.4 (87.3 to 91.5)</td>
</tr>
<tr>
<td>Fasting insulin, μU/mL</td>
<td>Before</td>
<td>18.1 (15.7 to 20.4)</td>
<td>16.6 (14.2 to 19.0)</td>
</tr>
<tr>
<td>Glucose AUC, mg/dL - min</td>
<td>Before</td>
<td>6057 (5221 to 6893)</td>
<td>6087 (5224 to 6951)</td>
</tr>
<tr>
<td>ISL0.120, mg - L²/mmol - μU - min</td>
<td>Before</td>
<td>74.4 (67.1 to 81.8)</td>
<td>70.9 (63.5 to 78.3)</td>
</tr>
<tr>
<td>QUICKI</td>
<td>Before</td>
<td>0.319 (0.313 to 0.325)</td>
<td>0.319 (0.313 to 0.325)</td>
</tr>
</tbody>
</table>

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; ISL0.120, insulin sensitivity index; AUC, area under the curve.

Table 4. Serum Lipids Before and After Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time</th>
<th>Treatment Group</th>
<th>P Value From Pairwise Comparison After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>Before</td>
<td>209 (198 to 220)</td>
<td>199 (188 to 211)</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>184 (177 to 199)</td>
<td>199 (192 to 205)</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>Before</td>
<td>128 (118 to 138)</td>
<td>122 (112 to 132)</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>128 (118 to 138)</td>
<td>122 (112 to 132)</td>
</tr>
<tr>
<td>High density lipoprotein</td>
<td>Before</td>
<td>55 (50 to 60)</td>
<td>53 (49 to 57)</td>
</tr>
<tr>
<td>cholesterol, mg/dL</td>
<td>After</td>
<td>54 (52 to 58)</td>
<td>51 (50 to 53)</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>Before</td>
<td>93 (81 to 106)</td>
<td>129 (117 to 142)</td>
</tr>
</tbody>
</table>

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 \(\leq 16\) 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. Fournier 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.

### Sources of Funding

This work was supported by grants from the National Heart, Lung, and Blood Institute (HL074103) and the General Clinical Research Center, National Institutes of Health (M01-RR-30). This publication was made possible by grant 5UL1RR024128-03 from the National Center for Research Resources, a component of the National Institutes of Health and the National Institutes of Health Roadmap for Medical Research.

### Disclosures

None.

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Hypertension. 2010;55:1199-1205; originally published online March 8, 2010; doi: 10.1161/HYPERTENSIONAHA.109.149153

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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