

Exercise and Weight Loss Reduce Blood Pressure in Men and Women With Mild Hypertension

Effects on Cardiovascular, Metabolic, and Hemodynamic Functioning

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Background: Lifestyle modifications have been recommended as the initial treatment strategy for lowering high blood pressure (BP). However, evidence for the efficacy of exercise and weight loss in the management of high BP remains controversial.

Methods: One hundred thirty-three sedentary, overweight men and women with unmedicated high normal BP or stage 1 to 2 hypertension were randomly assigned to aerobic exercise only; a behavioral weight management program, including exercise; or a waiting list control group. Before and following treatment, systolic and diastolic BPs were measured in the clinic, during daily life, and during exercise and mental stress testing. Hemodynamic measures and metabolic functioning also were assessed.

Results: Although participants in both active treatment groups exhibited significant reductions in BP relative to controls, those in the weight management group

generally had larger reductions. Weight management was associated with a 7-mm Hg systolic and a 5-mm Hg diastolic clinic BP reduction, compared with a 4-mm Hg systolic and diastolic BP reduction associated with aerobic exercise; the BP for controls did not change. Participants in both treatment groups also displayed reduced peripheral resistance and increased cardiac output compared with controls, with the greatest reductions in peripheral resistance in those in the weight management group. Weight management participants also exhibited significantly lower fasting and postprandial glucose and insulin levels than participants in the other groups.

Conclusions: Although exercise alone was effective in reducing BP, the addition of a behavioral weight loss program enhanced this effect. Aerobic exercise combined with weight loss is recommended for the management of elevated BP in sedentary, overweight individuals.

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HYPERTENSION IS a major health problem in this country, affecting more than 43 million people in the United States.¹ Hypertension is among the most common reasons for outpatient visits.² Despite this, blood pressure (BP) control is often inadequate.³ Although BP can be lowered pharmacologically in hypertensive individuals,^{4,5} antihypertensive medications are not effective for everyone, may be costly, and may induce adverse effects⁶⁻⁹ that impair quality of life and reduce adherence. Moreover, abnormalities associated with hypertension, such as insulin resistance and lipemia, may persist or may even be exacerbated by some antihypertensive medications.¹⁰⁻¹³ As a result, nonpharmacological approaches to the treatment of hypertension have received growing attention.

The 1997 report⁵ of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High

Blood Pressure recommends that lifestyle modifications be the initial treatment strategy for lowering high BP. Despite these recommendations, however, empirical data supporting the efficacy of exercise and weight loss in the management of hypertension are relatively limited. Numerous observational studies¹⁴⁻¹⁶ have demonstrated an inverse relation between physical activity and BP, and interventional studies^{17,18} have shown exercise to lower BP in normotensive individuals; however, there have been few randomized, controlled trials¹⁹⁻²² of exercise training in hypertensive individuals, and results have been mixed. Moreover, virtually all previous studies have important methodological shortcomings as none of the studies, to our knowledge, measured BP, physical fitness, or such potential confounding factors as age, body weight, or body composition in an optimal way, and study samples have been small and almost always excluded women.

SUBJECTS AND METHODS

SUBJECTS

Participants were recruited from newspaper, television, and radio advertisements; local clinics; and screenings at community health fairs and local shopping centers. Subjects were eligible if they were at least 29 years old and had an unmedicated high normal BP or stage 1 to 2 hypertension (mean clinic systolic BP [SBP] of 130-180 mm Hg and/or mean clinic DBP of 85-110 mm Hg on 4 separate occasions during a 3-week period). In addition, subjects were *sedentary* (not performing regular aerobic exercise) and *overweight* or *obese* (BMI, 25-37), as defined in the National Institutes of Health statement on obesity treatment.²⁹ Participants previously treated for hypertension were included if they had been taking no more than 1 medication that had been discontinued for at least 6 weeks. Reasons for subject exclusion included history of cardiac disease, secondary hypertension, renal disease, atrioventricular conduction defects or high-grade arrhythmias, valvular disease, severe asthma or chronic obstructive pulmonary disease, diabetes requiring insulin or hypoglycemic agents, and orthopedic problems that would preclude participation in aerobic exercise; a major psychiatric disorder requiring treatment; a comorbid medical condition that could require intensive treatment, such as cancer; use of any medications known to affect the cardiovascular system (antihistamines and decongestants); or a history of drug abuse or alcoholism. In this manner, 133 subjects, including 59 men and 74 women, 23% of whom were African American, were enrolled initially in the study (**Figure 1**).

STUDY DESIGN

This study was approved by the Institutional Review Board at Duke University Medical Center, Durham, NC, and informed consent was obtained from all subjects before their participation. Initial screening procedures included a medical history and a physical examination to rule out secondary hypertension and contraindications to exercise, in addition to the baseline assessment of clinic BP. At baseline, subjects also underwent assessment of BP on separate days during ABPM, physical exercise and mental stress testing, hemodynamic measurements, glucose tolerance testing, dietary assessment, and anthropometric measurements. Subjects were then randomized to 1 of 3 treatment conditions for 6 months: exercise only, weight management, or waiting list control. All measurements obtained at baseline were again obtained at the conclusion of the 6-month treatment program.

BP MEASUREMENTS

Clinic BP

Blood pressure measurements were obtained by a trained technician with a random zero sphygmomanometer and were standardized for cuff size and position. Measurements were made on 4 separate visits during a 3-week period. At each visit, BP was measured in the nondominant arm in the sitting position 4 successive times at 2-minute intervals after an initial rest period of 5 minutes. The first BP measurement of each visit was discarded, and the average of the remaining 3 measurements represented the

clinic visit BP. The overall clinic BP was then determined by averaging the mean BPs over the 4 visits. Measurements were obtained in this standardized manner at baseline and after 6 months.

Ambulatory BP Monitoring

The use of ABPM provides an opportunity to assess BP during routine activities of daily life. Because data from ABPM studies suggest that BP is highest during working hours,³⁰ subjects were studied during a typical workday. Subjects were hooked up between 8 and 10 AM to an ambulatory BP monitor (Accutacker II unit; Suntech, Raleigh, NC), and SBP and DBP recordings were verified by simultaneous manual readings. The ambulatory BP monitor measures BP noninvasively using the auscultatory technique, in which a microphone records and processes Korotkoff sounds; it uses electrocardiographic R-wave gating to correctly identify Korotkoff sounds originating from the brachial artery. The ambulatory BP monitor used has been validated independently.³¹ The monitor was programmed to obtain readings at an average frequency of 4 times per hour until bedtime. During ABPM, subjects were instructed to maintain a diary, which included information about their posture, mood, and activities. All ambulatory BP measurements were checked, and readings judged invalid (due to artifact) were excluded. The mean ambulatory SBP and DBP readings were then computed based on all remaining readings.

BP During Mental Stress

Blood pressure was measured using a monitor (exercise BP monitor, Accutacker model 4240; Suntech) during a mental stress protocol consisting of a 20-minute baseline rest period and 4 mental stress tasks with 10 minutes of rest between each. The tasks, presented in counterbalanced order, included: (1) public speaking, in which subjects were asked to give a 3-minute talk about a current events topic; (2) mirror image tracing, in which subjects had 3 minutes to outline a star, viewed in a mirror, as many times as possible without making any errors; (3) anger interview, in which subjects were given 3 minutes to relate an interpersonal situation that made them angry during the previous week; and (4) cold pressor, in which subjects placed 1 foot in a bucket of ice water for 2 minutes.

BP During Exercise Stress

Maximal exercise testing was performed using the Duke-Wake Forest protocol in which graded exercise began at 3.2 kilometers per hour and 0% grade and workload was increased at a rate of 1 metabolic equivalent per minute (oxygen, 3.5 mL/kg per minute).³² To ensure comparability in BP measurements during mental and exercise stress testing, the BP was obtained at each workload also using a monitor (exercise BP monitor, Accutacker model 4240; Suntech). Expired gases were collected for the determination of peak oxygen consumption using a metabolic cart (model 2900; Sensormedics, Yorba Linda, Calif).

RESTING HEMODYNAMICS

The hemodynamic determinants of BP, including heart rate (HR), CO, and TPR, were assessed by impedance

cardiography³³ during a 20-minute rest period. An impedance cardiograph (model H100-I; Hutcheson, Chapel Hill, NC) was used in conjunction with the standard tetrapolar band electrode configuration for signal acquisition. Two voltage electrode bands were applied, 1 around the base of the neck and 1 around the thorax at the tip of the xiphoid process; the 2 current electrode bands also were applied around the neck and chest, parallel to the voltage electrodes, with a constant distance of 4 cm above (neck) and below (chest) the voltage electrode bands. Impedance signals were recorded and processed using a recording program (Cardiac Output Program; Bio-Impedance Technology, Chapel Hill) that has been empirically validated.³⁴ The Kubicek equation³⁵ was used to compute stroke volume, and CO was computed as the product of HR and stroke volume. All impedance data were based on three 30-second samples of continuous data, which were recorded to correspond temporally to the 30-second periods of cuff deflations associated with BP measurements. Simultaneous measurement of CO and arterial BP allowed for the derivation of the TPR: TPR (measured as dynes times seconds per centimeters to the fifth power) = [mean arterial pressure (MAP)/CO] \times 80, where $MAP = DBP + [(SBP - DBP)/3]$.

GLUCOSE TOLERANCE TESTING

An oral glucose tolerance test was performed on each patient before and after the 6-month intervention. Participants fasted overnight, following which a heparin lock was inserted and blood drawn for fasting plasma glucose and insulin testing. Dextrose, 75 g, was administered orally, and samples for plasma glucose and insulin testing were obtained at 30-minute intervals for 3 hours. The glucose level was analyzed by hexokinase (model 800; Olympus, Melville, NJ) and by oxidase reduction (Ektachem/Vitros, Raritan, NJ). The plasma insulin level was analyzed by an insulin-specific radioimmunoassay (Linco Research, Inc, St Charles, Mo); the mean coefficients of variation for within- and between-assay variation were 3.2% and 3.9%, respectively.

DIETARY, WEIGHT, AND BODY COMPOSITION ASSESSMENT

To assess the relative contributions of exercise, dietary habits, and weight loss, an independent assessment of dietary content was obtained at baseline and at the conclusion of the intervention. Subjects recorded all food intake over 4 consecutive days in a diet diary that was analyzed for energy and nutritional content using computer software (Nutritionist IV software; N-Squared Computing, Salem, Ore).

Weight was measured by a standard balance scale. Body fat measurements were performed using a bioelectrical impedance analyzer (BIA-101Q; Quantum, Highland Heights, Ohio) in conjunction with bioelectrical impedance analyzer interpretation software (RJL Systems, Inc, Clinton Township, Mich). Measurements were done using standard right-sided, tetrapolar electrode placement with each subject in a supine position. Studies were conducted between 3 and 5 PM at ambient temperature following a standard protocol in which subjects had refrained from eating or drinking for at least 3 hours before testing.³⁶

INTERVENTIONS

Aerobic Exercise Only

Subjects exercised 3 to 4 times per week at a level of 70% to 85% of their initial HR reserve³⁷ determined at the time of the baseline treadmill test. The exercise routine consisted of 10 minutes of warm-up exercises, 35 minutes of cycle ergometry and walking (and eventually jogging), and 10 minutes of cool-down exercises. Subjects were instructed in how to monitor their radial pulses, and maintained their HRs at, or above, their target HRs for at least 30 minutes. A trained exercise physiologist supervised all exercise sessions, and performed 2 to 3 random checks of HRs per session to ensure that subjects were exercising at a sufficient intensity. Subjects were instructed to maintain their usual diets.

Weight Management

Subjects exercised 3 to 4 times per week using the identical protocol as previously described. In addition, subjects participated in a weight management program in small groups of 3 to 4 members. The weight management program was a behavioral intervention based on the LEARN manual,³⁸ which focuses on 5 elements: lifestyle, exercise, attitudes, relationships, and nutrition. The primary goal of the intervention was a weight loss of 0.5 to 1.0 kg/wk, achieved gradually by decreasing energy and fat intake through permanent lifestyle changes. Initial dietary goals were set at approximately 5021 J for women and 6276 J for men, with about 15% to 20% of this energy coming from fat. These values were flexible, however, and could be adjusted based on the rate of weight loss for each individual.

The program format consisted of approximately 26 weekly group sessions. At the start of each session, participants recorded their weight. Record keeping was a key component of the intervention, and all meetings began with a review of each member's food diary and homework (ie, behavior modification targets) from the previous week. Group participation was encouraged during this process in supporting fellow group members and in problem solving around obstacles and lapses that they may have encountered. After this review, new material from the manual, focusing primarily on behavior change strategies, was then introduced. This material included such topics as distinguishing cravings from hunger, planning healthy meals, shopping for food, dealing with pressures to eat, eating away from home, and coping with relapse. During the last part of each session, goals for the coming week were developed for each member and homework to help achieve these goals was assigned. During the last 6 weeks of the program, sessions focused increasingly on weight maintenance, and group members worked on individualized plans for maintaining the changes they had made during the past 6 months.

Waiting List Control

Subjects were asked to maintain their usual dietary and exercise habits for 6 months until they were reexamined. Waiting list subjects then selected either of the 2 active treatments on completion of their posttreatment assessment.

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DATA ANALYSIS

Baseline differences among treatment groups were assessed using 1-way analysis of variance for continuous variables and χ^2 tests for categorical variables. Treatment effects were evaluated using a multivariate analysis of variance, with posttreatment DBP and SBP serving as the dependent variables and treatment group as the factor. To examine potential differences between men and women in response to treatment, sex was also entered as a between-subjects factor. Separate multivariate analysis of variance models were estimated for clinic, ambulatory, mental stress, and exercise BPs and for each additional set of conceptually related variables (eg, glucose-related variables). Before each analysis, outcome measures were residualized on their respective pretreatment levels to adjust for baseline differences and to increase the precision of estimates. Within each model, planned contrasts were used to compare (1) the 2 treatment groups with controls and (2) weight management with exercise only. Following the intention-to-treat principle, posttreatment BP values were analyzed irrespective of patient adherence. In the event that some patients failed to return to the laboratory for their 6-month BP measurement, missing data were replaced with the corresponding pretreatment values.

Epidemiological studies have shown BP to be positively correlated with body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters), weight, and percentage body fat. Weight loss also has been shown to lower BP levels.²³ In a recent review, Jeffery²⁴ noted that there have been only 5 randomized, controlled trials of weight reduction for hypertension and that there is no research literature on weight loss treatments specifically for patients with hypertension. Furthermore, methodological limitations have proved to be significant. The uncontrolled use of antihypertensive medications, determination of BP from a single clinic visit, and failure to consider potentially important confounders, including measurement of exercise and dietary habits, have been especially problematic. Surprisingly, there have been only 2 studies of weight loss in unmedicated patients with mild hypertension, and results have been inconsistent. One study²⁵ showed no effect of weight loss on BP, while the other²⁶ demonstrated that subjects in a weight reduction group achieved greater declines in diastolic BP (DBP) than subjects receiving either placebo or metoprolol after 21 weeks of treatment. However, BP was determined on only 1 clinic visit, and neither exercise habits nor fitness levels were documented.

The present study examines the effects of exercise, alone and in combination with a behavioral weight loss program, on BP in a relatively large sample of unmedicated men and women with high BP. Because BP measured during routine activities of daily living may be more representative of an individual's BP level than clinic readings, patients also underwent ambulatory BP monitoring (ABPM) during waking hours. Blood pressure also

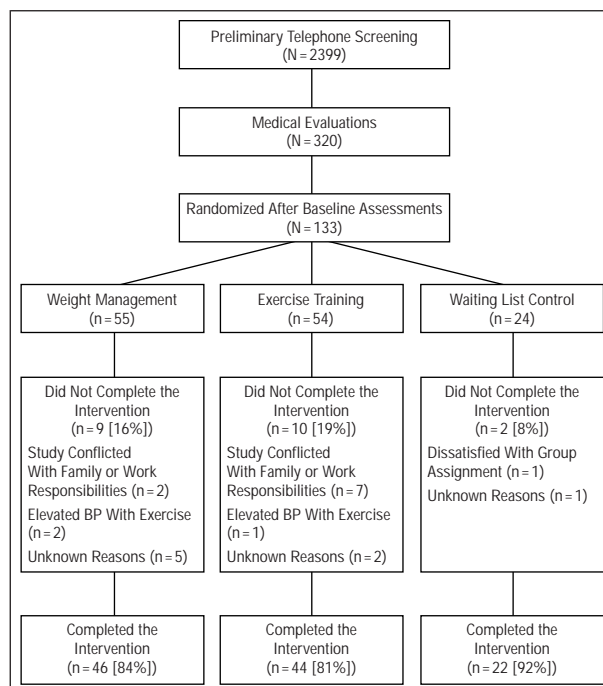


Figure 1. Patient flow from initial contact through completion of the intervention. BP indicates blood pressure.

was measured in a more controlled laboratory setting, during exercise, and during mental stress testing. Heightened mental stress-induced BP responses have been shown to be associated with myocardial ischemia²⁷ and future development of hypertension.²⁸ To gain insight into potential mechanisms by which BP was altered, participants also underwent glucose tolerance testing to assess insulin and glucose responses, body composition evaluations to determine body weight and fat distribution, assessment of dietary content, and noninvasive measurements of cardiac output (CO) and total peripheral resistance (TPR) to assess changes in hemodynamic profile.

RESULTS

BACKGROUND CHARACTERISTICS

Of the 133 subjects randomized, 112 participants (84%) completed the study, and an additional 9 of the 21 participants who dropped out of the treatment groups returned for follow-up assessment (Figure 1). There were no statistical differences across study groups on any baseline features, with the exception that participants in the exercise only group tended to have a lower clinic SBP at study enrollment compared with patients in the control group (**Table 1**). In addition, there were no sex-by-treatment interactions for any BP analysis.

ADHERENCE

Of the 54 participants in the exercise only group, 44 (81%) completed the full 26-week program, while 46 (84%) of the 55 participants in the weight management program completed the full program. Among the 24 control group participants, 22 (92%) were available for follow-up at the

Table 1. Background Characteristics*

Variable	Treatment Group			
	Weight Management (n = 55)	Exercise Only (n = 54)	Control (n = 24)	Entire Cohort (N = 133)
Males	21 (38)	25 (46)	13 (54)	59 (44)
Whites	44 (80)	41 (76)	15 (63)	100 (75)
Age, mean (SD), y	48.5 (1.2)	46.6 (1.2)	47.2 (1.8)	47.5 (0.77)
College degree	34 (62)	38 (70)	15 (63)	87 (65)
History of antihypertensive medicine use	17 (31)	12 (22)	4 (17)	33 (26)
Family history of hypertension	41 (75)	32 (59)	15 (63)	88 (68)
Clinic SBP, mean (SD), mm Hg	142.7 (1.4)	138.1 (2.1)†	143.8 (1.4)	141.0 (0.9)
Clinic DBP, mean (SD), mm Hg	93.2 (0.7)	93.6 (1.0)	94.4 (0.7)	93.6 (0.4)
Cardiac output, mean (SD), L/min	5.03 (1.6)	5.44 (1.8)	4.62 (1.1)	5.10 (1.6)
Total peripheral resistance, mean (SD), dyne · s · cm ⁻⁵	1785 (771)	1649 (671)	1889 (554)	1754 (696)
Fasting glucose level, mean (SD), mmol/L‡	4.82 (0.70)	4.80 (0.68)	4.76 (0.61)	4.80 (0.67)
Working outside of the home	50 (91)	51 (94)	21 (88)	122 (92)
Current smokers	2 (4)	5 (9)	2 (8)	9 (7)
Alcohol use, <1 serving/d	49 (89)	48 (89)	20 (83)	117 (91)

*Data are given as number (percentage) of subjects unless otherwise indicated. SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

†Significantly ($P < .05$) different from the control group.

‡To convert fasting glucose from millimoles per liter to milligrams per deciliter, divide millimoles per liter by 0.05551.

end of the 26-week study period. Including dropouts, participants in the weight management group attended an average of 73 (70%) of the 104 exercise training sessions; patients in the exercise only group attended an average of 80 (77%) of the exercise sessions ($P = .18$). Participants in the exercise only group exercised at or above their target HR training range 81% of the time, compared with 85% of the time for those in the weight management group ($P = .60$). Three participants in the exercise only group, and 4 in the weight management group, spent most of their exercise training using cycle ergometry rather than walking. When compared with participants who walked, the 7 who used the bicycle showed similar changes in oxygen consumption (walk, +11%; bicycle, +13%; $P = .48$) and treadmill time (walk, +12%; bicycle, +14%; $P = .61$).

CHANGES IN AEROBIC FITNESS

The groups differed significantly in posttreatment aerobic capacity and treadmill time (multivariate $F_{4,194} = 6.57$, $P < .001$). Participants in both active treatment groups were statistically different from controls on posttreatment peak oxygen consumption and treadmill time ($P < .001$ for both). The treatment groups also differed statistically from each other on treadmill time ($P = .04$), and there was a trend for greater peak oxygen consumption in the weight management group ($P = .07$) (**Figure 2**).

CHANGES IN BODY WEIGHT, BODY COMPOSITION, AND DIET

There were significant differences between the 3 groups in weight loss and postintervention BMI, percentage body fat, lean body mass, and lean-fat ratio (multivariate $F_{10,222} = 7.15$, $P < .001$). Participants in the weight management group exhibited an average weight loss of 7.8 kg, compared with a mean loss of 1.8 kg for those in the exercise only group and a mean gain of 0.7 kg for those in the control group. A similar pattern emerged

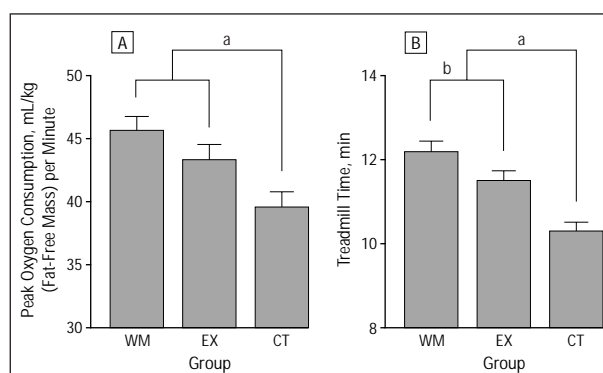


Figure 2. Aerobic fitness (A) and exercise tolerance (B) after treatment, adjusting for pretreatment levels. "a" indicates that weight management (WM) and exercise only (EX) participants differed from control subjects for peak oxygen consumption and treadmill time ($P < .001$ for both); "b," WM participants differed from EX participants for treadmill time ($P = .04$); and CT, waiting list control.

for BMI, percentage body fat, lean body mass, and lean-fat ratio, with participants in the weight management group showing larger changes than those in the exercise only group and controls showing virtually no change on these variables. Contrasts showed that the posttreatment weight, BMI, and percentage body fat were lower in the treatment groups compared with the control group. The lean body mass and lean-fat ratio were higher in the treatment groups compared with controls; the weight management group also exhibited a lower weight and BMI compared with the exercise only group (**Table 2**). In addition, a multivariate analysis of variance revealed significant treatment group effects for dietary variables (multivariate $F_{8,200} = 8.15$, $P < .001$). **Figure 3** shows that following treatment, those in the weight management group consumed less energy, less fat, and less protein than either those in the exercise only group or controls. There were no group differences for carbohydrate intake. In addition, those in the weight management group consumed less sodium after

Table 2. Changes in Weight and Body Composition

Variable	Treatment Time*	Treatment Group†			Contrast P‡	
		Weight Management	Exercise Only	Control	All Treatments vs Control	Weight Management Exercise Only
Weight, kg	Before	93.3 (17.7)	95.4 (14.5)	94.0 (17.3)	.92	.53
	After	85.4 (17.1)	93.6 (14.2)	94.7 (17.9)	.001	.001
	Change	-7.9 (6.0)	-1.8 (2.8)	0.7 (3.3)
BMI§	Before	32.1 (4.0)	32.8 (4.0)	32.6 (5.1)	.84	.44
	After	29.4 (4.5)	32.1 (4.0)	32.9 (5.4)	.001	.001
	Change	-2.7 (1.9)	-0.6 (0.9)	0.3 (1.1)
% Body fat	Before	34.3 (8.3)	35.1 (8.4)	34.0 (8.2)	.74	.61
	After	31.2 (8.8)	33.5 (9.7)	34.7 (8.5)	.002	.07
	Change	-3.2 (4.0)	-1.6 (4.7)	0.7 (2.0)
Lean body mass	Before	65.8 (8.3)	65.1 (8.4)	66.0 (8.2)	.74	.62
	After	68.9 (8.9)	66.7 (9.8)	65.3 (8.6)	.002	.07
	Change	3.2 (4.0)	1.6 (4.7)	-0.7 (2.0)
Lean-fat ratio	Before	2.1 (1.0)	2.1 (1.1)	2.1 (0.7)	.93	.63
	After	2.5 (1.1)	2.3 (0.6)	2.1 (0.8)	.02	.29
	Change	0.4 (0.7)	0.3 (0.6)	-0.1 (0.2)

*Differences between Before and After Values and Change scores are due to rounding.

†Data are given as mean (SD).

‡Contrasts for pretreatment means compare raw group means. Posttreatment means were compared after adjusting for pretreatment levels. Ellipses indicate data not applicable.

§BMI indicates body mass index, which is calculated as weight in kilograms divided by the square of height in meters.

6 months (3411 vs 2259 mg; $P < .005$), while consumption for those in the exercise only (3520 vs 3109 mg) and control (3116 vs 3039 mg) groups did not change. There also were no significant differences in the consumption of calcium ($P = .32$), potassium ($P = .93$), or magnesium ($P = .95$) among the groups.

CHANGES IN BP

Clinic BP

Comparison of posttreatment means revealed a significant difference among the groups (multivariate $F_{4,258} = 6.76$, $P < .001$). Planned contrasts revealed that both treatment groups had significantly lower SBPs and DBPs compared with the controls, while the 2 treatment groups did not differ significantly (**Figure 4**). Participants in the weight management group exhibited an average 7.4/5.6-mm Hg reduction in clinic SBP/DBP compared with a 4.4/4.3-mm Hg reduction for participants in the exercise only group and a 0.9/1.4-mm Hg change for controls.

Ambulatory BP

Posttreatment ambulatory BPs also were significantly different for the groups (multivariate $F_{4,256} = 5.45$, $P < .001$). The SBPs and DBPs were significantly lower in the active treatment groups compared with controls ($P = .02$ and $P = .002$, respectively) (**Figure 5**). In addition, compared with patients in the exercise only group, patients in the weight management group had a lower DBP ($P = .008$) and tended to have a lower SBP ($P = .11$).

Mental Stress BP

The groups differed significantly after treatment on BP at rest and during mental stress testing (multivariate

$F_{8,248} = 2.84$, $P = .005$). At rest, participants in both treatment groups had significantly lower SBPs and DBPs compared with controls ($P < .001$ for both); those in the weight management group also had lower DBPs than those in the exercise only group at rest ($P = .05$). During mental stress, those in the 2 treatment groups had significantly lower SBPs ($P < .001$) and DBPs ($P = .003$) than controls. Participants in the weight management group tended to have lower SBPs ($P = .15$) and DBPs ($P = .07$) compared with participants who only exercised (**Figure 6**).

Exercise Stress Testing BP

In multivariate analysis, there were no group differences in peak BP or BP at a submaximal (4 metabolic equivalents) workload (multivariate $F_{8,204} = 1.36$, $P = .21$) (**Table 3**). Similarly, contrasts at the univariate level showed that for peak exercise, there were no differences between the treatment groups and controls on SBP and DBP, and there were no differences between those in the weight management group and those in the exercise only group on SBP or DBP. At submaximal workloads, however, contrasts at the univariate level revealed that BPs were lower for those in the active treatment groups compared with controls for SBP. Participants in the weight management and exercise only groups did not differ on SBP ($P = .48$), but DBP tended to be lower for those in the weight management group than for those in the exercise only group.

GLUCOSE TOLERANCE TESTING

At baseline, the mean fasting glucose level for this sample was in the normal range, although 5% of subjects met the American Diabetes Association diagnostic criteria³⁹ for diabetes and 20% met criteria for glucose intolerance. There were no baseline group differences in glu-

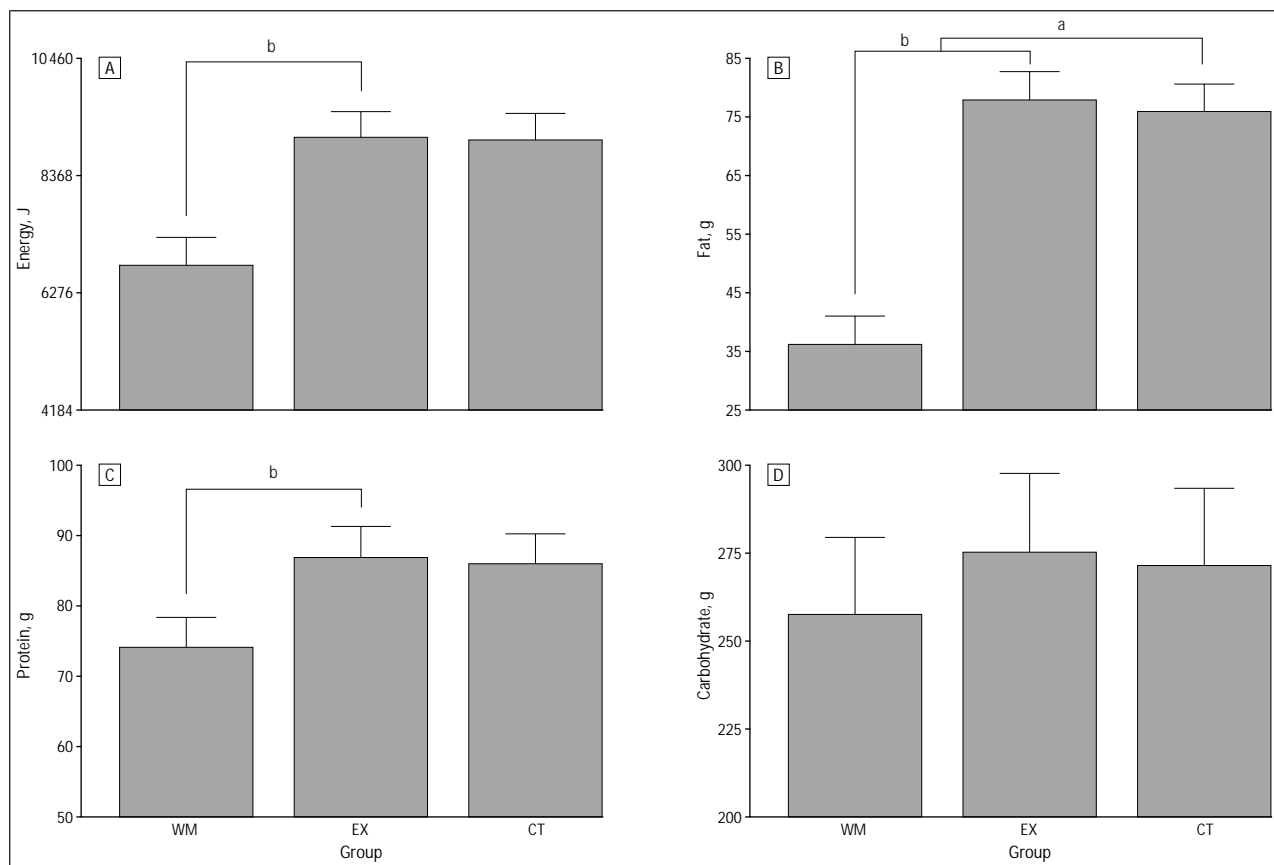


Figure 3. Dietary variables after treatment, adjusting for pretreatment levels. Energy consumption (A), fat intake (B), protein intake (C), and carbohydrate intake (D) are plotted separately. "a" indicates that weight management (WM) and exercise only (EX) participants differed from control subjects on fat intake ($P = .009$); "b," WM participants differed from EX participants on energy intake ($P < .001$), fat intake ($P < .001$), and protein intake ($P = .01$); and CT, waiting list control.

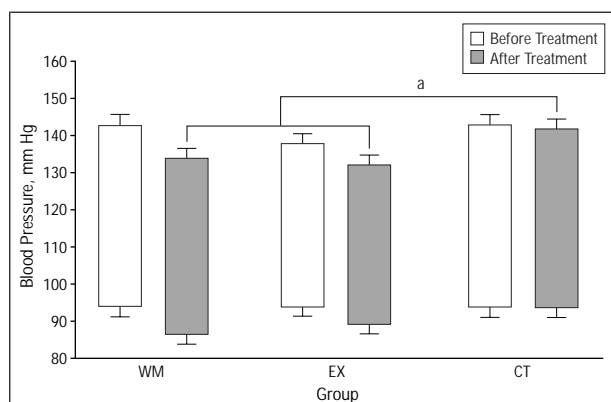


Figure 4. Observed clinic blood pressure before and after treatment. Groups were compared on blood pressure following treatment after adjusting for pretreatment levels. "a" indicates that weight management (WM) and exercise only (EX) participants differed from control subjects for systolic ($P = .001$) and diastolic ($P < .001$) blood pressure; CT, waiting list control.

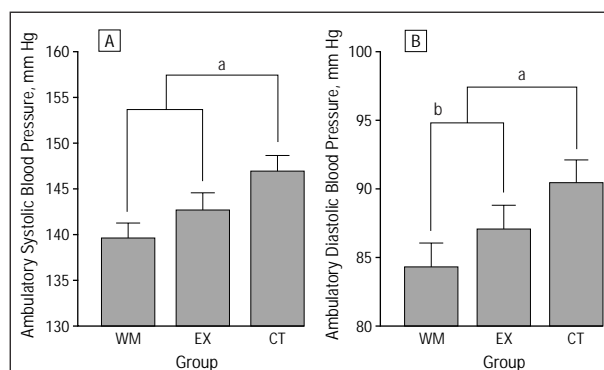


Figure 5. Ambulatory systolic (A) and diastolic (B) blood pressure after treatment, adjusting for pretreatment levels. Blood pressure was determined during waking hours. "a" indicates that weight management (WM) and exercise only (EX) participants differed from control subjects on ambulatory systolic ($P = .02$) and diastolic ($P = .002$) blood pressure; "b," WM participants differed from EX participants on diastolic blood pressure ($P = .008$); and CT, waiting list control.

cose or insulin levels in the fasting state or in response to an oral dextrose load, represented by the incremental glucose and insulin areas measured over time. This area under the curve above the fasting glucose or insulin level provides a single number that illustrates the plasma glucose and insulin secretory response to a nutrient load. As shown in **Table 4**, there were significant group differences in fasting glucose and insulin levels, and in the

area under the curve for glucose and insulin (multivariate $F_{8,206} = 2.86$, $P = .005$), after treatment.

Subjects in the weight management group had significantly lower fasting glucose levels after treatment than subjects in the exercise only group. Subjects in the weight management group also had marginally significantly lower posttreatment fasting insulin levels than those in the exercise only group.

For the posttreatment glucose area under the curve, contrasts revealed that subjects in the active treatment groups tended to have lower glucose areas than controls; however, subjects in the weight management group had particularly lower glucose areas compared with those in the exercise only group. Similarly, for the insulin area under the curve, those in the active treatment groups tended to have lower areas than controls, and the value for those in the weight management group was lower than for those in the exercise only group (Table 4). **Figure 7** shows that the changes in glucose and insulin levels were larger for those in the weight management group than for those in the exercise only and control groups.

RESTING HEMODYNAMIC MEASURES

The groups also differed significantly after treatment on resting MAP, HR, CO, and TPR (multivariate $F_{8,196} = 4.96$, $P < .001$). **Figure 8** shows that participants in both ac-

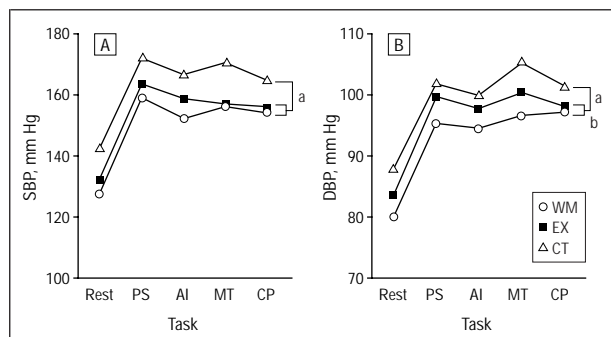


Figure 6. Systolic blood pressure (SBP) (A) and diastolic blood pressure (DBP) (B) at rest and during mental stress tasks following treatment, adjusting for pretreatment levels. "a" indicates that weight management (WM) and exercise only (EX) participants differed from control subjects for SBP and DBP at rest and during all stress ($P < .05$ for all); "b," WM participants differed from EX participants for DBP at rest ($P = .05$); PS, public speaking; AI, anger interview; MT, mirror trace; CP, cold pressor; and CT, waiting list control.

tive treatment groups were different from controls on MAP ($P < .001$), HR ($P = .003$), CO ($P = .01$), and TPR ($P = .004$). The MAP was lower for those in the weight management group than for those in the exercise only group ($P = .05$); those in the weight management group also had a lower TPR compared with those in the exercise only group ($P = .04$). Those in the weight management and exercise only groups did not differ significantly from each other on HR ($P = .50$) or CO ($P = .28$).

COMMENT

The results of this clinical trial of exercise and weight loss among men and women with an elevated BP indicate that while exercise alone is effective in reducing SBP and DBP, the addition of a behavioral weight loss program significantly augments the efficacy of aerobic training. The reduction in resting clinic BP was approximately 4 mm Hg for SBP and DBP in participants in the exercise only group compared with 7 mm Hg for SBP and 5 mm Hg for DBP in participants in the weight management group. Larger BP reductions also were observed for those in the weight management group relative to those in the exercise only group with ABPM during routine activities of daily living, particularly for DBP. In addition, BP levels were lower for those in the exercise only and weight management groups relative to controls during mental stress and submaximal exercise. Those in the weight management group also tended to have larger DBP reductions than those in the exercise only group during mental stress and submaximal exercise.

These results contrast with those of a previous study²⁰ in which exercise alone was not associated with significant BP reductions after 4 months of exercise training. The reasons for this discrepancy can be attributed to important methodological differences between the 2 studies, including different patient characteristics (<20% vs 10%-50% above ideal body weight) and a more ex-

Table 3. Changes in Blood Pressure During Exercise*

Variable	Treatment Time†	Treatment Group‡			Contrast P		
		Weight Management	Exercise Only	Control	All Treatments vs Control	Weight Management vs Exercise Only	
Peak BP, mm Hg							
	Systolic	Before	221.1 (20.8)	224.0 (25.0)	224.4 (22.5)	.73	.32
	After	225.2 (20.5)	226.8 (23.3)	228.2 (18.8)	.63	.66	
	Change	4.1 (23.6)	2.8 (23.2)	3.8 (22.1)	
Diastolic	Before	95.3 (14.7)	94.1 (13.2)	94.6 (11.2)	.84	.96	
	After	94.3 (16.2)	93.3 (11.7)	92.8 (9.0)	.59	.82	
	Change	-1.0 (13.9)	-0.7 (12.1)	-1.8 (11.2)	
BP at 4 METs, mm Hg							
	Systolic	Before	191.6 (22.4)	192.6 (24.2)	193.0 (16.2)	.95	.88
	After	181.8 (27.1)	184.4 (21.0)	191.9 (19.8)	.03	.45	
	Change	-9.7 (18.7)	-8.2 (17.3)	-1.0 (20.1)	
Diastolic	Before	96.2 (11.5)	93.4 (10.5)	93.3 (10.0)	.96	.10	
	After	90.8 (10.9)	92.6 (10.2)	94.9 (10.7)	.07	.08	
	Change	-5.4 (11.0)	-0.8 (11.3)	1.6 (9.7)	

*BP indicates blood pressure; MET, metabolic equivalent; and ellipses, data not applicable.

†Differences between Before and After values and Change scores are due to rounding.

‡Data are given as mean (SD).

Table 4. Changes in Glucose and Insulin Levels

Variable	Treatment Time*	Treatment Group†			Contrast P‡	
		Weight Management	Exercise Only	Control	All Treatments vs Control	Weight Management vs Exercise Only
Fasting level, µU/mL						
Glucose	Before	86.9 (12.6)	86.5 (12.2)	85.8 (11.0)	.45	.99
	After	82.8 (9.0)	88.8 (18.3)	90.3 (11.4)	.13	.009
	Change	-4.0 (10.3)	2.2 (13.5)	4.5 (6.7)
Insulin	Before	17.1 (8.5)	19.3 (11.6)	21.3 (12.8)	.65	.20
	After	13.5 (5.7)	19.3 (16.5)	21.6 (11.2)	.21	.05
	Change	-3.5 (6.0)	-1.0 (14.1)	0.3 (7.0)
Area under the curve, mg · min/dL						
Glucose	Before	7297 (3943)	6441 (3921)	6021 (3861)	.42	.51
	After	5392 (3133)	6080 (3459)	6708 (3862)	.10	.02
	Change	-1904 (3218)	-361 (2770)	687 (2630)
Insulin	Before	11 187 (7035)	9839 (6587)	13 272 (8265)	.40	.86
	After	6948 (4700)	9075 (6996)	13 025 (9715)	.07	.005
	Change	-4239 (6549)	-765 (5246)	-248 (5629)

*Differences between Before and After values and Change scores are due to rounding.

†Data are given as mean (SD).

‡Values are unadjusted. Contrasts for pretreatment means compare unadjusted group means; posttreatment means were compared after adjusting for pretreatment levels. Ellipses indicate data not applicable.

tended exercise program (4 vs 6 months). Most significantly, while the within-group BP changes were comparable among the exercisers in the 2 studies, the waiting list control group in the previous study exhibited a significant BP reduction after 4 months, while the BP for the waiting list control group in the present study remained unchanged. This difference could be attributed to a greater stability in BP as a result of the added number of qualifying BP measurements.

The results of the present study are comparable generally with findings from 5 other randomized clinical trials. In a Finnish study⁴⁰ of 34 normotensive men and 25 hypertensive men randomized to 4 months of either exercise or observation, the exercise and control groups had similar 8–mm Hg reductions in DBP, but exercise was associated with larger decreases in SBP (9 vs 0 mm Hg). However, the exercisers also lost significant weight, which was not controlled for in the analysis. In a study of 20 Japanese men with hypertension,⁴¹ subjects who exercised for 10 weeks exhibited a 12/5–mm Hg BP reduction, whereas control subjects showed no change in BP. In a third study⁴² of 56 hypertensive men, BP decreased 12/7 mm Hg among exercisers compared with a decrease of 6 mm Hg in SBP and an increase of 3 mm Hg in DBP among controls. In a fourth study⁴³ of 27 hypertensive men, exercisers exhibited a BP reduction from 137/95 to 130/85 mm Hg after 10 weeks, while the control group showed no change (135/94 to 136/94 mm Hg). The changes in DBP, but not SBP, were significantly different. However, both groups showed comparable changes in body weight and aerobic fitness. Finally, Gordon and colleagues⁴⁴ randomized 55 sedentary, overweight patients with high normal BP or stage 1 or 2 hypertension to exercise only, diet (reduced energy), or exercise and diet for 12 weeks. Clinic BP reductions in the combination group (12.5/7.9 mm Hg) were larger than those in the diet only (11.3/7.5 mm Hg) and exercise alone

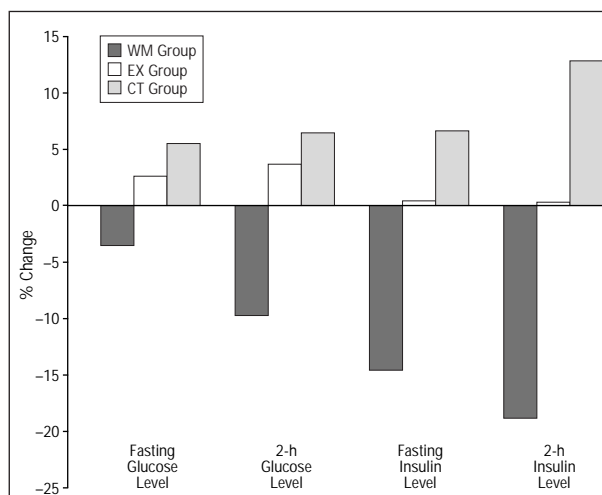


Figure 7. Percentage change in fasting and 2-hour glucose and insulin levels. WM indicates weight management; EX, exercise only; and CT, waiting list control.

(9.9/5.9 mm Hg) groups. However, because results failed to reach statistical significance, the researchers concluded that the BP-lowering effects of exercise and weight loss were not additive.

Taken together, these previous studies present a mixed picture. One study²⁰ showed comparable BP reductions in exercisers and controls; 2 studies found BP reductions in both groups, but one⁴⁰ found larger SBP, but not DBP, changes in the exercise group, whereas the other⁴³ found larger DBP, but not SBP, changes in the exercise group; and 2 other studies^{41,42} found larger BP reductions in the exercise group relative to controls. The final study⁴⁴ lacked a control group, and did not have sufficient statistical power to detect group differences. In addition, all of the studies were limited because of high drop-out rates, unplanned crossover, imprecise measurement

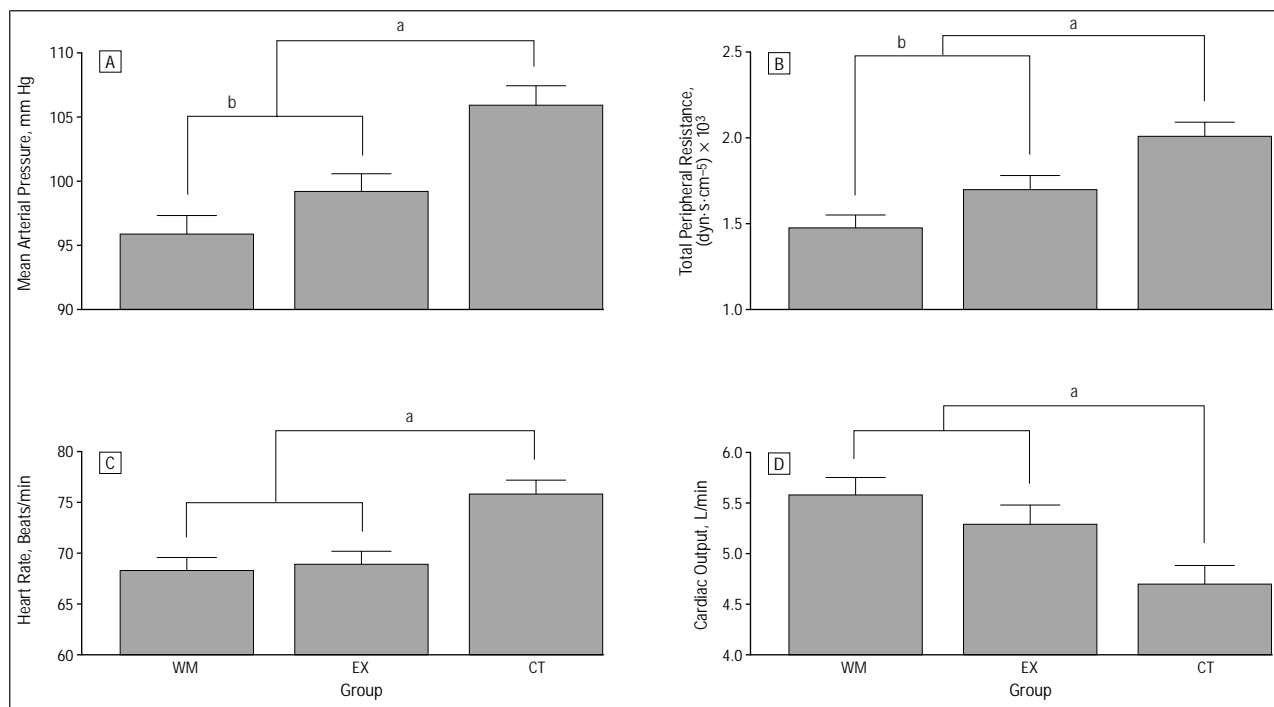


Figure 8. Resting hemodynamic measures after treatment, adjusting for pretreatment levels. Mean arterial pressure (A), total peripheral resistance (B), heart rate (C), and cardiac output (D) are plotted separately. "a" indicates that weight management (WM) and exercise only (EX) participants differed from control subjects on mean arterial pressure ($P < .001$), heart rate ($P = .003$), cardiac output ($P = .01$), and total peripheral resistance ($P < .001$); "b," WM participants differed from EX participants on mean arterial pressure ($P = .05$) and total peripheral resistance ($P = .04$); and CT, waiting list control.

of BP or aerobic fitness, or failure to precisely measure other potential confounders. Moreover, only 2 studies^{20,44} included women. The present study suggests that exercise is associated with modest BP reductions, independent of weight loss, and, in the absence of sex-by-treatment interactions, that women and men achieve significant exercise-related BP reductions. Furthermore, findings indicate that moderate exercise by itself is generally not associated with significant weight loss, and that adding a behavioral weight loss program to an exercise intervention results in even greater BP reductions than the reductions observed with exercise alone. Indeed, while changes in aerobic fitness were correlated with changes in SBP ($r = -0.21$, $P = .04$) and DBP ($r = -0.27$, $P = .007$), weight loss was even more highly correlated with SBP and DBP changes ($r = 0.38$ and 0.44 , respectively; $P < .001$ for both). These BP reductions are not only statistically significant but are clinically meaningful: 22 (67%) of the 33 participants engaging in exercise and weight loss who met criteria⁵ for stage 1 hypertension (SBP, 140-159 mm Hg, or DBP, 90-99 mm Hg) at baseline were no longer hypertensive (SBP, < 140 mm Hg, and DBP, < 90 mm Hg) after treatment compared with 13 (43%) of the 30 who only exercised and 2 (12%) of the 17 controls. When participants with stage 2 hypertension were included (SBP, 160-179 mm Hg, or DBP, 100-109 mm Hg), 23 (55%) of 42 participants in the weight management group, 13 (37%) of 35 participants in the exercise only group, and 2 (11%) of 19 participants in the control group were no longer hypertensive.

The exercise and weight loss interventions resulted in a lowering of BP that was due to a reduction in TPR. Before randomization to the intervention groups,

hypertension in our study sample was characterized hemodynamically by an elevated TPR. This hemodynamic profile is typical of patients with established hypertension, although some studies⁴⁵ have shown that obese patients with hypertension may have a less elevated TPR than lean patients with hypertension. Nevertheless, the exercise and weight loss interventions resulted in reduced BPs secondary to lowered TPRs, which is consistent with the target hemodynamic response for anti-hypertensive therapy, and the intervention is, therefore, considered to have had a therapeutic hemodynamic effect.

The intervention also improved the metabolic profile of subjects, but primarily those in the weight management group. After treatment, weight management participants exhibited significantly lower fasting and postprandial glucose and insulin levels, indicating improved insulin sensitivity. In contrast, exercise only participants and waiting list controls did not develop improved insulin sensitivity, showing virtually no change from baseline on either insulin or glucose variables. The failure of aerobic exercise alone to affect glucose levels is consistent with other data showing no enduring effect of such training on glucose metabolism, despite the positive effects on glucose associated with acute aerobic exercise and resistance training.^{46,47} Moreover, the few studies⁴⁸ that have shown improvements in glucose control after exercise training have not clearly demonstrated whether these effects are due to exercise independent of weight loss. For the effects of exercise training on insulin sensitivity, independent of weight loss, the picture is even less clear. Although the present study found little effect of exercise alone on insulin sensitivity, previous reports⁴⁶⁻⁴⁸ have shown that aerobic exercise im-

proves insulin sensitivity in certain patient populations, such as in individuals with type 2 diabetes mellitus. However, the beneficial effects of exercise on insulin sensitivity appear to be short lived,^{46,49} and have been found to have no independent effect after controlling for the effects of recency of exercise and changes in body composition.^{50,51} These factors also may explain the lack of any substantial effect of exercise training alone on insulin sensitivity in the present study.

Our sample of individuals with an elevated BP was relatively young (mean age, 47 years), educated (65% obtained a college degree), employed (92% were working), and receptive to nonpharmacological approaches to reduce BP. The extent to which less motivated persons with fewer socioeconomic resources would adhere to a diet and exercise program is unknown, particularly if the program was not delivered in a highly structured and supervised setting. Moreover, because both active treatment groups engaged in exercise, we could not determine the effects of weight loss alone.

In summary, the present findings suggest that while exercise training alone is effective in reducing BP, the addition of a behavioral weight loss program significantly enhances this effect. Moreover, a combined program of exercise and weight loss contributes to additional benefits, such as larger BP reductions during mental stress and submaximal exercise and improved insulin sensitivity, that are clinically meaningful. Combining a program of exercise and weight loss is recommended for the management of overweight individuals with an elevated BP.

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