Abstract African American women have a high prevalence of insulin resistance, non–insulin-dependent diabetes mellitus, obesity, and hypertension that may be linked to low levels of physical activity. We sought to determine whether 7 days of aerobic exercise improved glucose and insulin metabolism in 12 obese (body fat >35%), hypertensive (systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 mmHg) African American women (mean age 51±8 years). Insulin-assisted frequently-sampled intravenous glucose tolerance tests were performed at baseline and 14 to 18 hours after the 7th exercise session. There was no significant change in maximal oxygen consumption,
body composition, or body weight after the 7 days of aerobic exercise. The insulin sensitivity index increased (2.68±0.45 · 10^-5 to 4.23±0.10 · 10^-5 [min^-1/pmol/L], P=.02). Fasting (73±9 to 50±9 pmol/L, P=.02) and glucose-stimulated (332±58 to 261±45 pmol/L, P=.05) plasma insulin levels decreased. Additional measures related to the insulin resistance syndrome also changed with the 7 days of exercise: basal plasma norepinephrine concentrations were reduced (2.46±0.27 to 1.81±0.27 nmol/L, P=.02) and sodium excretion rate increased from 100±13 to 137±7 mmol/d (P=.03); however, there was no change in potassium excretion or 24-hour ambulatory blood pressure. We conclude that a short-term aerobic exercise program improves insulin sensitivity in African American hypertensive women independent of changes in fitness levels, body composition, or body weight. The present study indicates that short-term exercise can improve insulin resistance in hypertensive, obese, sedentary African American women and confirms previous reports that a portion of the exercise-induced improvements in glucose and insulin metabolism may be the result of recent exercise.

Key Words: insulin sensitivity • exercise • blacks

Introduction

Coexistent hypertension and NIDDM is more common among African Americans than whites.1–3 Specifically, African American women have some of the highest rates of insulin resistance, NIDDM, obesity, and hypertension.4–7 In general, physical activity has been shown to be associated with insulin sensitivity and lower rates of NIDDM, obesity, and hypertension. When compared with other ethnic groups in the United States, African American women have low levels of physical activity.23 Therefore, it is possible that low levels of physical activity in African American women may play a role in their high prevalence of hypertension and NIDDM.

Long-term endurance exercise training improves insulin sensitivity and reduces both fasting and glucose-stimulated plasma insulin levels.8,11,12,21,22,34,35 However, changes in (VO\textsubscript{2max}), body composition, and/or body weight may also occur with long-term exercise training, all of which are independently associated with changes in insulin sensitivity. We previously used short-term exercise training to demonstrate significant reductions in fasting and oral glucose–stimulated insulin levels.18,19 This short-term exercise model is useful in that improvements in glucose and insulin metabolism are observed in a relatively short period of time without changing VO\textsubscript{2max}, body composition, or body weight. Previous short-term exercise training studies in normotensive whites did not obtain measures of insulin sensitivity. It is not known whether short-term exercise training improves insulin sensitivity without changing VO\textsubscript{2max}, body composition, or body weight in populations with high rates of insulin resistance and
physical inactivity, such as hypertensives or African Americans. Therefore, the present study was undertaken to examine the effect of short-term exercise training on insulin sensitivity in obese, hypertensive African American women.

Reaven suggested a mechanistic model whereby insulin resistance leads to hyperinsulinemia with subsequent increases in plasma NE levels, sodium reabsorption, and arterial BP. Thus, the high prevalence of insulin resistance in African Americans may explain their high prevalence of essential hypertension. We also sought to obtain preliminary information regarding the effects of the exercise intervention on those components of the insulin resistance syndrome that may be related to the development and maintenance of hypertension.

### Methods

The study group consisted of African American women (n=12) ranging in age from 40 to 63 years (Table 1). Volunteers were recruited from the Pittsburgh area through newspaper advertisements and public service announcements. The study was approved by the Biomedical Institutional Review Board of the University of Pittsburgh Medical Center. All subjects provided written informed consent.

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Volunteers were excluded if they had cardiovascular disease, liver or renal disease, or diabetes (fasting glucose level >7.8 mmol/L). All volunteers were nonsmokers and were not participating in regular physical activity. Two subjects were being treated with antihypertensive medications and gradually were tapered off their medication and studied after a minimum of 4 weeks of no medication therapy. Subjects had a physical examination, routine fasting blood chemistries, and BP measured under standardized conditions. Specifically, BP was determined on 4 separate days over 2 weeks by auscultation. Subjects were included in the study if their casual systolic BP was ≥140 mmHg and/or their diastolic BP was ≥90 mmHg (Table 1). A graded maximal exercise treadmill test (Naughton protocol) was performed to screen for coronary heart disease and to determine $\dot{V}O_2$max.

**Baseline Testing**
After completing the screening, subjects had their body composition measured using dual-energy x-ray absorptiometry (model DPX-L; Lunar Radiation Corp) following an overnight fast and after voiding completely. Subjects then met with a GCRC dietitian to select food items typical of their usual diet. The food selections were used to develop a diet for each subject. The diets were prepared by the GCRC so that, for each subject, a diet that was identical in composition, calories, and electrolytes to their usual diet was consumed before and during both testing periods. The carbohydrate content of the diet was 250 to 300 g/d, and the sodium content was based on each subject's typical dietary sodium intake as determined by a dietary interview and analysis by the research dietitian.

**Frequently Sampled Intravenous Glucose Tolerance Test**

To assess whole-body insulin sensitivity before and after the exercise intervention, subjects underwent two insulin-assisted FSIVGTTs according to the methods of Bergman. Both FSIVGTTs were performed at the GCRC starting between 7:00 and 8:00 AM on the morning after the third day of the diet. All subjects fasted for >10 hours before the start of each FSIVGTT. The second FSIVGTT was administered 14 to 18 hours after the last exercise session.

Indwelling catheters were inserted into the antecubital veins bilaterally. One catheter was used for administration of glucose and insulin, and the other was used for drawing blood samples; both were maintained patent with a slow saline drip. After a 30-minute equilibration period, three basal blood samples for glucose and insulin were drawn. d-Glucose (300 mg glucose/kg as 50% dextrose) was injected over a 1-minute period. Insulin (0.02 U/kg, Humulin-Regular, Eli Lilly Inc) was injected 20 minutes after the glucose injection to augment the insulin response. Sufficient saline flush was used to guarantee total delivery of the glucose and insulin doses. Blood samples for glucose and insulin were drawn at 28 standard time points for 3 hours after the glucose injection. Additional blood samples were drawn for measurement of plasma NE concentration after 30 minutes of supine rest (fasting sample) and at 10 and 30 minutes after the glucose injection. These time points were chosen to assess the plasma NE response to increased plasma insulin levels.

Blood samples were placed in a glycolytic inhibitor and anticoagulant, stored temporarily on ice, and then centrifuged at 4°C. Plasma samples for insulin obtained during the first FSIVGTT were stored at −70°C. To control for interassay variability, all insulin measurements were performed at the end of the study. Insulin was measured by radioimmunoassay, and glucose was measured by the glucose oxidase method (YSI Glucose Analyzer, Yellow Springs). NE was measured with a radiometric assay. The glucose and insulin data were analyzed using the Bergman Minimal Model (MINMOD) program to determine the insulin sensitivity index (SI). Intravenous glucose tolerance (KG) was calculated as the slope of the regression line relating the logarithm of glucose concentration to time between 10 and 19 minutes after the glucose injection. The acute insulin response to glucose (AIRG) was calculated as the mean plasma insulin concentration during the first 10 minutes after glucose injection minus the basal plasma insulin concentration.
24-Hour Urine Collection
On the third day of their diet, both before and after the 7-day exercise intervention, subjects began a urine collection after their first void in the morning. The urine collection period ended after their first void the next morning. Urine samples were analyzed for sodium and potassium using the ion-selected electrode technique (Vitros 250, Johnson & Johnson).

Exercise Intervention
Although some studies in young, healthy individuals demonstrated improved glucose uptake after a single exhaustive bout of exercise in which muscle glycogen stores were significantly diminished,16,17 this is not the case in older, less fit individuals.18,19 Consecutive days of exercise have been found previously to cause a cumulative depleting effect on muscle glycogen stores.15 In the present study, exercise consisted of 7 consecutive days of treadmill walking and cycle ergometry. In addition, we have found previously that 7 days of exercise does not alter \( \overline{V}O_2 \text{max} \), body weight, or body composition.18,19 Each exercise session began with a 10-minute warm-up consisting of walking and stretching exercises. The subjects then walked on a treadmill for 30 minutes, followed by 5 minutes of rest, and then 20 additional minutes of treadmill walking or cycle ergometry. A heart rate monitor (Polar CIC, Inc) was used to ensure that each subject's exercise heart rate corresponded to 65% of their heart rate reserve. After completing the exercise intervention, subjects underwent the same testing as performed during the baseline testing period.

Ambulatory BP Monitoring
To obtain preliminary data on the effect of the short-term exercise intervention on BP, 7 subjects underwent 24-hour ambulatory BP monitoring using a noninvasive BP monitor (SpaceLabs Medical Inc, model 90219) at baseline and again after the exercise intervention. The monitor was calibrated against a conventional sphygmomanometer before each session. An eighth exercise session was performed on the same day of the FSIVGTT. The second ambulatory BP monitoring period began the next morning 14 to 18 hours after the eighth exercise session. This was done so that insulin sensitivity and ambulatory BP were assessed during the same period after the preceding exercise session. Subjects were instructed not to exercise outside of the laboratory before or during either monitoring period and to pause momentarily and maintain their body position during each BP measurement. For the baseline 24-hour period, subjects recorded their activity at each BP measurement. For the 24-hour recording period after the intervention, subjects were given a copy of their activity record and instructed to repeat it as closely as possible. The ambulatory BP monitor automatically edited BP readings outside the default limit established by the manufacturer (BP >260/150 mmHg, pulse pressure >150 mmHg, and heart rate >200 beats/min). The ambulatory BP monitor calculated 24-hour average BP and 12-hour average day and night BP (day: 6:00 AM to 6:00 PM; night: 6:00 PM to 6:00 AM).

Data Analyses
Data were analyzed with standard statistical software (STATVIEW, Super ANOVA, Abacus Concepts). Differences between baseline and after the exercise intervention were tested with a Student's paired \( t \) test.
A repeated-measures ANOVA model was used to test for differences in ambulatory BP. All data are presented as mean±SEM. A significance level of $P \leq 0.05$ was accepted for statistical significance.

## Results

The average duration and intensity during the exercise sessions were 51±1 minutes and 65±1% of heart rate reserve, respectively. Seventy-five percent of each exercise session consisted of walking, and the remaining time consisted of stationary cycling. After the exercise intervention, there were no significant changes in body weight, body composition, or $\dot{V}O_2$max.

### Glucose and Insulin Metabolism

Fasting glucose levels were unchanged (4.8±0.4 versus 4.9±0.3 mmol/L); however, fasting insulin levels were significantly reduced after the 7 days of exercise (73±9 to 50±9 pmol/L, $P=0.05$).

The baseline $S_I (2.68\pm0.50 \cdot 10^{-5} \text{[min}^{-1}/\text{pmol/L}]$) increased by 58% ($P=0.03$) to 4.23±1 \cdot 10^{-5} (min^{-1}/pmol/L) after the 7-day exercise intervention (Figure [2]). Eleven of the twelve subjects were initially insulin-resistant ($S_I < 3.0$) as defined by Bergman et al [14]; however, after 7 days of exercise, only 6 subjects remained insulin-resistant. At baseline, mean $K_G$ was 0.91±0.64%/min, which is considered to be low glucose tolerance. $K_G$ did not change significantly from baseline (0.91±0.64 versus 0.83±0.58%/min), which is similar to other exercise studies that found significant improvements in insulin sensitivity and insulin secretion without significant changes in glucose tolerance [8,11,12,21,22,34,35]. Glucose-stimulated insulin secretion, measured as the acute insulin response to glucose (AIR$_G$), was reduced by 21% from 332±58 to 261±45 pmol/L ($P=0.05$) after the 7 days of exercise.
Factors Associated With Insulin Resistance Syndrome
Twenty-four-hour urinary sodium excretion was higher (137±7 versus 100±13 mmol/d, *P*=.03) and 24-hour urinary potassium excretion was unchanged (58±8 versus 59±8 mmol/d) after exercise (Table 2). Fasting plasma NE concentration was reduced by 26% (2.46±0.27 versus 1.81±0.27 nmol/L, *P*=.02) after the exercise intervention. Plasma NE levels increased during the first 30 minutes of both FSIVGTTs, but the sum of plasma NE concentration during the FSIVGTT after the exercise intervention was significantly reduced by 28% from 5.93±0.85 to 4.29±0.73 nmol/L (*P*=.03). There were no significant changes in day or night systolic and diastolic ambulatory BP.

**Discussion**
In the present study, we found that insulin sensitivity was improved by 58% after 7 consecutive days of exercise in sedentary, obese, hypertensive African American women. This improvement in insulin sensitivity was associated with 20% and 25% reductions in fasting and glucose-stimulated plasma insulin.
levels. We did not observe a change in intravenous glucose tolerance. These results are consistent with our previous studies that demonstrated reduced fasting and glucose-stimulated insulin responses in older men and women with the same 7-day exercise model. It is possible that our previously demonstrated reductions in insulin responses were mediated by an increase in insulin sensitivity. This is confirmed in the present study as evidenced by the 58% improvement in S1 from the FSIVGTT.

A number of previous studies from our and other laboratories have demonstrated that long-term exercise training improves insulin sensitivity and reduces fasting and glucose-stimulated insulin levels in a wide range of individuals. However, in most of these studies exercise training also reduced body weight and body fat and improved \( \dot{V}O_2 \) max, which can directly influence insulin sensitivity. As in our previous studies, the benefit of the 7-day exercise intervention model is that no changes in \( \dot{V}O_2 \) max, body fat, or body weight occurred, which made it possible to assess the independent effects of exercise.

Kahn et al previously used the FSIVGTT and Bergman's Minimal Model technique to assess the effects of exercise training on glucose and insulin metabolism in older normotensive men. These men reduced their body fat by 11% and increased their \( \dot{V}O_2 \) max by 18% with 6 months of exercise training at 80% to 85% of heart rate reserve. The FSIVGTT after 6 months of exercise training was administered 2 to 3 days after the last exercise training session. Thus, this study eliminated the acute effect of exercise from consideration and quantified only the effects of improved body composition and cardiovascular fitness on glucose and insulin metabolism. Their improvements in insulin and glucose metabolism are almost identical to those resulting from only 7 consecutive days of exercise in the present study. Their fasting insulin levels decreased by 21%, whereas the reduction in the present study was 32%. Their reduction in AIRG was 23%, whereas in the present study AIRG was reduced by 21%. The improvements in insulin sensitivity in the present study were greater than those of Kahn and coworkers (58% versus 36%, respectively). The difference in the magnitude of improvement in insulin sensitivity between the present study and the study by Kahn et al may be due to the amount of time between the last exercise session and the second FSIVGTT. In the present study, the second FSIVGTT was performed 14 to 18 hours, as opposed to 2 to 3 days, after the last exercise session. The results of the present study support the contention that recent exercise can have a substantial impact on glucose and insulin metabolism. Additionally, the magnitude of this effect may be comparable to the effect that substantial improvements in body composition and cardiovascular fitness resulting from long-term exercise training can have on glucose and insulin metabolism.

To our knowledge, this is the first demonstration that exercise improves insulin sensitivity in African American women. Middle-aged and older African American women have among the highest rates of obesity and NIDDM in the world. They are also much less physically active than their peers from other ethnic groups. These reduced physical activity levels may be critical in the etiology of the
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Elevated rates of NIDDM and hypertension in this group, as evidenced by the fact that only 7 days of exercise resulted in a substantial improvement in their insulin sensitivity. Insulin sensitivity in the overall group improved from the impaired to only slightly below normal range. In addition, dramatic improvements on an individual basis occurred in 5 subjects. These improvements occurred without any long-term adaptations to exercise training such as changes in VO2 max, body weight, or body composition. These data emphasize the need to assess the role of increased physical activity to potentially ameliorate the high rate of NIDDM and hypertension in this especially affected subset of the US population.

These significant improvements in insulin sensitivity and plasma insulin levels with the 7 consecutive days of exercise allowed us to obtain preliminary data regarding possible associations between improvements in plasma insulin levels and insulin sensitivity and other components of the Insulin Resistance Syndrome. It has been shown previously that acute hyperinsulinemia causes sodium retention. Therefore, we sought to determine whether the exercise-induced reduction in plasma insulin levels would be associated with increased sodium excretion rates. Subjects in the present study increased their sodium excretion rates by 27% after 7 days of exercise despite the fact that dietary intake of electrolytes remained constant for the 2 days before and the day of both urine collection periods. A number of long-term exercise training studies in hypertensives have also demonstrated alterations in electrolyte metabolism. Our data indicate that alterations in sodium balance may occur early in the exercise training program.

Previous studies have reported decreased indices of sympathetic nervous system activity after long-term exercise training in hypertensive and normotensive individuals. In the present study, plasma NE levels were used as an index of sympathetic nervous system activity. Basal and insulin-stimulated plasma NE levels were significantly lower after the 7 consecutive days of exercise. The present data indicate that this response may occur very rapidly in hypertensives at the initiation of an exercise training program, similar to normotensives.

Reaven's insulin resistance syndrome is based on the hypothesis that insulin resistance causes hypertension by increasing plasma insulin levels, thereby increasing sympathetic nervous system activity and renal sodium reabsorption. In the present study, despite the fact that both sodium excretion and plasma NE levels were improved, there were no changes in ambulatory BP. One previous study reported improved insulin sensitivity and decreased insulin levels with 14 weeks of exercise training in hypertensive individuals. Our data support their finding that although insulin sensitivity was improved, ambulatory BP did not change. One explanation is that because the time course of these adaptations was not assessed in the present study, the improvements in sodium excretion and plasma NE levels could have been evident for anywhere from 1 to 7 days. Thus, it is possible that the improvements in these pressor mechanisms may not have been present long enough to affect ambulatory BP. A second explanation is that sodium excretion and/or sympathetic nervous system activity are not the mechanistic links between...
hyperinsulinemia and hypertension.

There are some limitations to the present study. First, the sympathetic nervous system is activated in a regional rather than a global manner. The measurement of plasma NE levels provides only an indirect measure of sympathetic nervous system activity. Second, the sample size for the measurement of ambulatory BP was small and, therefore, no definitive conclusions may be made. Additional studies are necessary to assess the effects of improvements in insulin sensitivity and insulin levels on NE kinetics and to determine whether alterations in insulin sensitivity and insulin levels affect renal sodium handling.

In summary, these results indicate that 7 consecutive days of exercise produce substantial improvements in insulin sensitivity and fasting and glucose-stimulated plasma insulin levels in insulin-resistant hypertensive African American women. This finding is important because African American women have high rates of insulin resistance, NIDDM, and hypertension. These improvements in glucose and insulin metabolism occurred in the absence of concomitant changes in $\dot{V}O_2$ max, body weight, or body composition, thus indicating that decreased physical activity per se may play a critical role in the high rate of NIDDM and hypertension in this population. Additionally, the magnitude of the changes in glucose and insulin metabolism observed in the present study is comparable to that observed after 6 months of exercise training. The implication is that exercise-induced improvements in insulin sensitivity may occur in two ways: (1) an adaptation to long-term exercise training due to improved fitness levels and body composition or reduced body weight; or (2) an acute response to recent exercise possibly due to reduced muscle glycogen stores. Higher sodium excretion rates and lower plasma NE levels were associated with an improvement in insulin sensitivity; however, ambulatory BP was not affected by short-term exercise in these insulin-resistant hypertensive African American women.

### Selected Abbreviations and Acronyms

- **BP** = blood pressure
- **FSIVGTT** = frequently sampled intravenous glucose tolerance test
- **GCRC** = General Clinical Research Center
- **NE** = norepinephrine
- **NIDDM** = non–insulin-dependent diabetes mellitus
- **$\dot{V}O_2$ max** = maximal oxygen consumption
Acknowledgments

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References

Figure 1. Individual measurements of insulin sensitivity index (SI) at baseline and after 7 days of aerobic exercise training.