Hypertension (HTN) is a major health problem. Each year, 7.1 million deaths worldwide are attributed to HTN. In the United States, >62% of adults have above-optimal blood pressure (BP). One in five people with pre-HTN will develop HTN within 4 years of diagnosis, and nearly all middle-aged Americans will acquire HTN if they live long enough. The current costs attributed to HTN are $76.6 billion annually in the United States with antihypertensive medications accounting for approximately 38% of this amount. These trends and expenditures underscore the importance of treating high BP with lifestyle interventions such as physical activity.

Regular participation in physical activity reduces the risk of developing HTN and cardiovascular disease (CVD). Habitual physical activity is also associated with other health benefits that favorably modulate HTN and CVD. Aerobic exercise training reduces BP by 5 to 7 mm Hg. Some if not all of the magnitude of the BP reductions resulting from aerobic exercise training arises from sustained BP reductions that occur immediately following individual bouts of physical activity. This phenomenon is referred to as post-exercise hypotension (PEH).

Because of the documented acute (ie, immediate) and chronic (ie, training) BP lowering benefits of exercise, the American College of Sports Medicine recommends people with high BP perform a minimum of 30 minutes of moderate intensity (40%-60% VO2peak) aerobic exercise on most days of the week. Nonetheless, investigations examining the influence of the level of physical exertion (ie, exercise intensity) on PEH are limited. Our group and others found lower intensity (30%-60% VO2peak) was as effective as more rigorous intensity (60%-75% VO2peak) aerobic exercise in immediately reducing post-exercise BP.
However, Quinn, Forjaz et al, and Smelker et al found bouts of vigorous exercise intensity (~75% VO2peak) elicited greater BP reductions than lower intensity bouts (~50% VO2peak).17,19 These discrepant findings suggest a more individualized approach to prescribing exercise intensity for those with HTN may be warranted.

The primary purpose of this study was to continue our investigation of the influence of exercise intensity on PEH by examining a range of levels of physical exertion (low, 40% VO2peak; moderate, 60% VO2peak; and vigorous, 100% VO2peak) compared to non-exercise control among middle-aged, men with pre-to Stage 1-HTN. Consistent with our prior work,11,12 we hypothesized exercise bouts of low and moderate exercise intensity would be as or more effective in eliciting PEH than a bout of vigorous intensity aerobic exercise. A secondary purpose was to explore clinical biomarkers associated with PEH in order to gain insight into the clinical characteristics of people most likely to lower their BP with exercise.

Methods

Subjects

Subjects in this investigation were from the same cohort of our previous publications.11,12,20-26 They were 45 white, nonsmoking men 18-55 years old. Volunteers were apparently healthy other than having pre- to stage 1 HTN [systolic BP (SBP) 130 ≤ 160 mm Hg and/or diastolic BP (DBP) 85 ≤ 100 mm Hg]. Subjects were excluded if they had CVD, diabetes mellitus, asthma, thyroid dysfunction, pancreatitis, acute illness and/or were on antidepressant medication. Any subject taking medications for the treatment of high BP was asked to discontinue usage for four weeks before participation. If the withdrawal of antihypertensive medications was shown to result in a resting SBP ≥ 160 mm Hg and/or DBP ≥ 100 mm Hg, the individual was excluded from study participation. Subjects completed an informed consent approved by the institutional review boards of the University of Connecticut and Hartford Hospital before participating.

Study design and procedures

The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents. This work was supported by an American Heart Association grant (0150507N). The methods of this investigation have been published and are summarized briefly.11,12,20-26

Initially, volunteers completed an orientation session to familiarize themselves with study protocols and ensure they met the study inclusion criteria. Seated resting BP was measured in the left then right arm three times with 5 minutes between measurements to determine BP status. Height (cm) and weight (kg) were used to calculate body mass index (kg m-2). Waist circumference (cm) indicated central adiposity.

At the end of the orientation session, subjects left the laboratory attached to an ambulatory BP monitor (Accutracker II automatic noninvasive ambulatory BP monitor, Suntech Medical Instruments Inc, Raleigh, NC) to confirm BP status. The participants were instructed to proceed with their usual activities, avoid formal exercise, keep their arm still during BP measurements, and wear the monitor until waking the following morning. The same investigator attached the ambulatory BP monitor to all participants. A calibration check was completed with a mercury sphygmomanometer using a t-tube following the manufacturer’s guidelines.

The ambulatory BP monitor took BP measurements randomly three times every hour during awake hours from 6 AM to 11 PM, and once an hour during sleeping hours between 11 PM to 6 AM. The computerized recordings were accepted if at least 80% of the potential BP readings were obtained. Values were deleted if they met the following quality control rejection criteria: SBP >220 mm Hg and <80 mm Hg, DBP >130 mm Hg and <40 mm Hg, and pulse pressure >110 mm Hg and <20 mm Hg. The monitor was programmed to obtain a second reading if there was a change between consecutive readings of SBP >50 mm Hg, DBP >40 mm Hg, and pulse pressure >50 mm Hg.

Participants completed four experiments: a non-exercise control session of seated rest and three cycle exercise bouts on an upright cycle ergometer performed at 40% VO2peak (LOW), 60% VO2peak (MODERATE), and 100% VO2peak (VIGOROUS) (Figure 1). All experiments were conducted at the same time of day to account for diurnal variation in BP; however, blinding was only possible until the conclusion of the baseline period due to the nature of the study design. Subjects sat quietly for a 20 minutes baseline period at the start of each experimental session. The same investigator measured heart rate (HR), SBP, and DBP on each subject for each experiment. During the baseline period, HR was recorded using a Polar Accurex Plus HR monitor (Polar Electro Inc, Port Washington, NY) every 2 minutes, while SBP and DBP were measured every other minute by auscultation. Each experiment was followed by a 45 minutes recovery period in the seated position with BP and HR measured every 2 and 3 minutes, respectively. Subjects were attached to the ambulatory BP monitor after experiments until waking the following morning.

VIGOROUS (100% VO2peak) consisted of a graded cardiopulmonary exercise stress test (Monark Ergomedic 818E, Stockholm, Sweden). VO2peak was determined by breath-by-breath analysis of expired gases during testing via an open circuit respiratory apparatus (Sensormedics Vmax 29 Metabolic Cart, SensorMedics Corp, Yorba Linda, CA). The graded exercise stress test began with a resistance of 0.5 kp (50 W) and consisted of continuous cycling at a constant cadence (60 rev/ minutes) with the resistance increased 0.5 kp every 2 minutes until volitional exhaustion. During VIGOROUS, HR was recorded continuously with a 12-lead electrocardiogram system (Marquette Case 8000, Jupiter, FL), and BP was measured every 2 minutes by auscultation. Results of the peak graded cardiopulmonary exercise stress test (VIGOROUS) were used to calculate the intensity of the remaining experimental exercise sessions and exclude subjects with coronary artery disease.

Each volunteer performed the three remaining experiments in random order: non-exercise control, LOW (40% VO2peak), and MODERATE (60% VO2peak). The nonexercise control was a 40-minute session of seated rest. LOW and MODERATE consisted of a 5-minute warm-up of freewheeling with no resistance, 30 minutes of cycling at the designated exercise intensity, and a 5-minute cool-down period to total 40 minutes of exercise. HR, SBP, and DBP were measured every 5 minutes during nonexercise control, LOW, and MODERATE.
Blood sampling and analyses

All blood samples were drawn without stasis from the antecubital vein of the right arm using a 20 gauge, 32 mm indwelling Teflon catheter. The cannulas were kept patent with a solution of 0.9% saline. Blood samples were taken prior to the experimental sessions for fasting blood lipid-lipoproteins, insulin, and glucose. Blood samples were also obtained at the conclusion of the experimental baseline periods for C-reactive protein (CRP), plasma fibrinogen (FIB), and renin. Blood samples were drawn into anticoagulated EDTA tubes and centrifuged at 3000 RPM at 4°C for 15 minutes. Plasma samples were transferred into storage tubes and frozen at-80°C until analysis.

Fasting plasma glucose concentrations were determined in duplicate by an automated glucose oxidase method (Yellow Springs Instruments, Model 2003, Yellow Springs, OH). The intra- and interassay coefficient of variation (CV) for the fasting plasma glucose determinations were 2.8% and 3.6%, respectively, at 4.7 mmol·L⁻¹. Fasting plasma concentrations of insulin were determined by radioimmunoassay with a solid phase, single antibody assay in duplicate (Coat-a-Count Insulin, TKN2, Diagnostic Products Corporations, Los Angeles, CA). The intra- and interassay CV for measuring plasma insulin concentrations were 7.0% and 7.8%, respectively. Fasting blood lipid-lipoproteins were determined by oxidase assays using colorimetric...
enzymatic methods (Cobras Integra, Roche Diagnostics, Mannheim, Germany). The intra- and inter-assay CV for these assays were 1.6% and 1.9%, respectively. Low density lipoprotein (LDL) was calculated with the Friedwald equation.27

Baseline CRP concentrations were measured via particle-enhanced immunoturbidimetry on the Cobras Integra analyzer (CRP latex cassette, Roche Diagnostic Corporation, Indianapolis, IN) with low, normal, and high quality control values. The intraassay CV for CRP was 3.22%, 3.85%, and 3.66%, respectively. Baseline FIB levels were determined in duplicate with the Diagnostica Stago kit (Parsippany, NJ). The intra-and inter-assay CV for plasma FIB level determinations were 3.4% and 3.7%, respectively. Baseline direct renin concentrations were measured by immunoradiometric assay (Diagnostic Systems Laboratories, Inc, Webster, TX) with a sensitivity of 0.48 μU·mL⁻¹. Assays were performed with low-, normal-, and high-quality control values in a commercial laboratory (Quest Diagnostics).

Statistical analyses
Descriptive statistics (means ± SEM) were calculated for all study variables. The ambulatory BP difference from baseline at hourly intervals after the experimental sessions over the course of 9 h was calculated and averaged. The 9h observation period was chosen for this study because it represents the time over which all men were awake and ambulating and so that similar comparisons could be made with our previous work.11,12,20-26 Repeated measure analysis of variance (RMANOVA) examined if ambulatory BP differed over time among experiments (nonexercise control, LOW, MODERATE, and VIGOROUS). Simple linear regression was used to determine the relationship between the magnitude of the BP change from baseline over 9 h and exercise intensity. Multiple linear regression examined clinical determinants of the SBP and DBP post-exercise response following VIGOROUS since our findings following LOW and MODERATE have been published.20-25 All statistical analyses were performed with the Statistical Package for Social Sciences Version 14.0 for Windows (SPSS Inc, Chicago, IL) with P < .05 established as the level of statistical significance.

Results
Subjects
Subjects were 45 white, middle-aged men with pre-to Stage 1 HTN (Table I). The participants were overweight to obese and had borderline dyslipidemia and below-average physical fitness.29 The SBP, DBP, and HR responses before, at peak exercise, and >9 h following VIGOROUS are shown in Table II. No subject exhibited a hypertensive response to the graded exercise test as defined by the American College of Sports Medicine as SBP >250 mm Hg and/or DBP >115 mm Hg.29

Systolic blood pressure
Over the course of 9 h, SBP increased after LOW and MODERATE and decreased after VIGOROUS from a baseline of 127.7 ± 1.7 mm Hg (Table III, Figure 2) (P < .010). SBP tended to increase an average of 2.7 ± 1.6 mm Hg less after LOW (P = .087) versus non-exercise control. Furthermore, SBP increased an average of 5.4 ± 1.4 mm Hg less after MODERATE and 11.7 ± 1.5 mm Hg less after VIGOROUS (P < .001) compared to non-exercise control with the magnitude of the difference greater after VIGOROUS than MODERATE and LOW (P < .010). Linear regression revealed for each 10% increase in relative exercise intensity, SBP was reduced by 1.5 mm Hg (Figure 4) (P < .010).

Diastolic blood pressure
Over the course of 9 h, DBP decreased after LOW, MODERATE, and VIGOROUS from a baseline of 87.5 ± 1.1 mm Hg (Table III, Figure 3) (P < .010). DBP tended to decrease an average of 1.5 ± 1.2 mm Hg more after LOW (P = .207) and 2.0 ± 1.0 mm Hg more after MODERATE (P = .055) versus non-exercise control. In addition, DBP decreased 4.9 ± 1.3 mm Hg more after VIGOROUS (P < .001) compared to non-exercise control with the magnitude of the difference greater after VIGOROUS than MODERATE and LOW (P < .010). Linear regression demonstrated for each 10% increase in relative exercise intensity, DBP was lowered by 0.6 mm Hg (Figure 4) (P < .010).

Clinical correlates of the BP response after VIGOROUS
Results from the multiple linear regression of correlates of the BP response following VIGOROUS are displayed in Table IV as reduced models with only significant or influential factors retained. This model accounted for 40.0% of the variation in the post-exercise SBP response (P = .002). Fasting blood glucose, baseline CRP, and baseline renin levels were the strongest correlates of the SBP response following VIGOROUS. The model also explained 42.9% of the variability in the post-exercise DBP response (P = .001). VO2peak, fasting LDL, and baseline renin were the strongest correlates of the DBP response following VIGOROUS.

<table>
<thead>
<tr>
<th>Table I. Mean ±SEM clinical characteristics of the subjects (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
</tr>
<tr>
<td>Body mass index (kg·m⁻²)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
</tr>
<tr>
<td>Awake systolic blood pressure (mm Hg)</td>
</tr>
<tr>
<td>Awake diastolic blood pressure (mm Hg)</td>
</tr>
<tr>
<td>Peak oxygen consumption (mL·kg⁻¹·min⁻¹)</td>
</tr>
<tr>
<td>Baseline fibrinogen (mg·dL⁻¹)</td>
</tr>
<tr>
<td>Baseline C-reactive protein (mg·L⁻¹)</td>
</tr>
<tr>
<td>Renin (μU·mL⁻¹)</td>
</tr>
<tr>
<td>Fasting glucose (mmol·L⁻¹)</td>
</tr>
<tr>
<td>Fasting insulin (pmol·L⁻¹)</td>
</tr>
<tr>
<td>Fasting low-density lipoproteins (mg·dL⁻¹)</td>
</tr>
<tr>
<td>Fasting high-density lipoproteins (mg·dL⁻¹)</td>
</tr>
<tr>
<td>Fasting triglycerides (mg·dL⁻¹)</td>
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<tr>
<td>Access here for more details.</td>
</tr>
</tbody>
</table>
The primary purpose of this investigation was to examine the influence of a range of levels of physical exertion on PEH. Our new and unexpected findings were that VIGOROUS (SBP/DBP, 11.7/4.9 mm Hg) elicited the largest BP reductions followed by MODERATE (5.4/2.0 mm Hg) and then LOW (2.8/1.5 mm Hg) compared to nonexercise control over the course of 9 h among men with pre- to stage 1 HTN. The influence of exercise intensity on PEH occurred in dose response fashion such that for each 10% increase in relative VO2peak SBP decreased 1.5 mm Hg and DBP 0.6 mm Hg. Our findings are consistent with growing literature reporting greater CVD health benefits from participation in vigorous versus moderate to lower intensity aerobic exercise. These greater exercise intensity associated CVD health benefits

### Table II. Systolic and diastolic blood pressure, and heart rate (mean ± SEM) before, at peak exercise, and over 9 hours after VIGOROUS (95% CI) [n = 45]

<table>
<thead>
<tr>
<th>Hemodynamic variable</th>
<th>Before</th>
<th>Peak exercise</th>
<th>Over 9 h after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>135.1 ± 1.7 (131.6-138.7)</td>
<td>221.6 ± 3.1 (215.3-227.9)</td>
<td>131.6 ± 2.3 (126.9-136.3)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>90.0 ± 1.2 (87.6-92.5)</td>
<td>88.9 ± 1.7 (85.4-92.4)</td>
<td>80.0 ± 1.6 (76.8-83.2)</td>
</tr>
<tr>
<td>Heart rate (beat·min⁻¹)</td>
<td>72.9 ± 1.7 (69.3-76.4)</td>
<td>179.1 ± 1.7 (175.7-182.4)</td>
<td>72.9 ± 2.2 (68.5-77.3)</td>
</tr>
</tbody>
</table>

### Table III. Blood pressure change (mean ± SEM) from baseline after exercise and nonexercise control over 9 h (95% CI)

<table>
<thead>
<tr>
<th>SBP response (mm Hg)</th>
<th>Control</th>
<th>Low</th>
<th>Moderate</th>
<th>Vigorous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>127.7 ± 1.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-pre-experimental change</td>
<td>10.7 ± 1.3 (8.1-13.3)</td>
<td>7.9 ± 1.3 (5.3-10.5)</td>
<td><strong>5.3 ± 1.4</strong> (2.5-8.1)</td>
<td><strong>10.7 ± 1.7</strong> (8.1-13.3)</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>-1.4 ± 0.9 (95% CI)</td>
<td>-2.9 ± 0.8 (95% CI)</td>
<td>-3.5 ± 0.8 (95% CI)</td>
<td><strong>−6.3 ± 1.2</strong> (95% CI)</td>
</tr>
<tr>
<td>Moderate</td>
<td>-3.3 ± 0.5 (95% CI)</td>
<td>-4.5 ± 1.3 (95% CI)</td>
<td>-5.1 ± 1.8 (95% CI)</td>
<td>-8.8 ± 3.8 (95% CI)</td>
</tr>
<tr>
<td>Vigorous</td>
<td>-4.5 to 2.5 (95% CI)</td>
<td>-5.1 to 1.8 (95% CI)</td>
<td>-8.8 to −3.8 (95% CI)</td>
<td></td>
</tr>
</tbody>
</table>

Baseline is the blood pressure average (± S.E.M.) of the pre-experiment 20-minute period of seated rest; Post-pre-experiment change = mean of the hourly blood pressure averages over the course of 9 hours after the experiments minus average baseline blood pressure.

* P < .001 compared to the non-exercise control.

### Figure 2

Awake systolic blood pressure change from baseline (mean ± SEM) at hourly intervals over 9 h after control and exercise compared with baseline values. CONTROL, non-exercise session of seated rest. * P < .001 exercise treatment versus non-exercise control.

### Figure 3

Awake diastolic blood pressure change from baseline (mean ± SEM) at hourly intervals over 9 h after control and exercise compared with baseline values. * P < .001 exercise treatment versus non-exercise control.
include lower BP, reduced blood lipid-lipoproteins, improved glucose use, more favorable body composition, and greater risk reduction in CVD and all-cause mortality.7,13,30,31 Thus, a more individualized approach to prescribing exercise intensity may be warranted for those with pre-to stage 1 HTN to optimize the magnitude of the BP lowering effects and associated CVD health benefits resulting from aerobic exercise.

We also explored clinical correlates of the SBP and DBP responses following VIGOROUS since our findings following MODERATE and LOW have been published.22-25 Fasting blood glucose, baseline renin, and baseline CRP levels were the strongest correlates of the SBP response following VIGOROUS. Baseline renin, fasting LDL, and VO2peak were the strongest correlates of the DBP response following VIGOROUS. These models explained 40.0% and 42.9% of the variability in the SBP and DBP response, respectively. These results suggest potential mechanistic clues for PEH that are consistent with our previous work and others indicating involvement of the renin angiotensin system6,7,24,32 and modulation of PEH by cardiometabolic, inflammatory, and hemostatic biomarkers.6,22,25,33-35

This investigation is one of the first to examine the influence of a range of exercise intensity on PEH. Surprisingly, we found exercise intensity exerts a dose response on PEH with the more vigorous bouts eliciting the largest BP reductions. The finding of VO2peak explaining 18.6% of the DBP response over 9 h following VIGOROUS is in agreement with our earlier work following MODERATE22 that the magnitude of PEH was greatest in the more physically fit men after higher levels of physical exertion. Clinical translation of advocating vigorous intensity exercise as antihypertensive therapy is challenging as adverse cardiovascular and orthopedic effects are more likely to occur with vigorous than moderate to low levels of physical exertion, especially in those who are irregularly physically active.29,30,37 Nonetheless, acute vigorous exercise participation is relatively safe with an absolute risk of sudden cardiac death estimated at one per year for every 15,000-18,000 people.29,36,37 Our findings indicate clinicians should prescribe exercise for elevated BP on a person-by-person basis. Thus, caution and good judgment should be used when prescribing more vigorous exercise for those with high BP. Our findings also suggest the current American College of Sports Medicine exercise prescription recommendations for people with HTN regarding exercise intensity should be expanded to include more vigorous levels of physical exertion for those who are willing and able to tolerate more intense levels of exercise.7

This study is subject to several limitations. The inclusion criteria for study volunteers were purposely restrictive in order to limit the possible confounding influences of age, sex, ethnicity, medication, and disease state on PEH. However, the inclusion criteria also limit the clinical translation of findings to women, other ethnic groups, and younger and older populations. Our results are hypothesis generating and should be confirmed in a larger, more ethnically diverse sample of men and women across the lifespan. Furthermore, our findings suggesting involvement of the renin angiotensin and sympathetic nervous systems and cardiometabolic, inflammatory and hemostatic biomarkers in PEH should be probed in future investigations to better elucidate PEH mechanisms.

In conclusion, PEH occurred in dose response fashion with the level of physical exertion of the exercise bout. For each 10% increase in relative VO2peak, SBP decreased 1.5 mm Hg and DBP 0.6 mm Hg. However, clinicians will need to weigh the intensity related dose response BP lowering effects of aerobic exercise against the potentially more adverse effects of vigorous exercise when prescribing exercise to lower BP among those with HTN. Thus, a more individualized approach to prescribing exercise intensity may be warranted for those with pre-to stage 1 HTN to optimize the magnitude of the BP

**Table IV.** Multiple linear regression of the clinical correlates of the blood pressure response following VIGOROUS

<table>
<thead>
<tr>
<th>Variable</th>
<th>R</th>
<th>P</th>
<th>Variable</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose</td>
<td>-0.415</td>
<td>.011</td>
<td>VO2peak</td>
<td>-0.431</td>
<td>.006</td>
</tr>
<tr>
<td>Baseline C-reactive protein</td>
<td>-0.362</td>
<td>.028</td>
<td>Baseline low</td>
<td>-0.431</td>
<td>.006</td>
</tr>
<tr>
<td>Baseline renin</td>
<td>-0.348</td>
<td>.035</td>
<td>Baseline renin</td>
<td>-0.411</td>
<td>.009</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>0.310</td>
<td>.062</td>
<td>Baseline fibrinogen</td>
<td>0.369</td>
<td>.021</td>
</tr>
<tr>
<td>Fasting low-density lipoprotein</td>
<td>-0.298</td>
<td>.074</td>
<td>Fasting glucose</td>
<td>-0.326</td>
<td>.043</td>
</tr>
</tbody>
</table>
lowering effects and associated CVD health benefits resulting from aerobic exercise for those who are willing and able to tolerate more intense levels of exercise.

Acknowledgements

We thank the subjects who volunteered their time, corporate and municipal agencies who enabled subject recruitment, and the University of Connecticut graduate students who assisted with data collection.

Disclosures

Conflict of Interest: None.

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