American Journal of Epidemiology
Copyright © 2006 by the Johns Hopkins Bloomberg School of Public Health
All rights reserved; printed in U.S.A.

Vol. 163, No. 10
DOI: 10.1093/aje/kwj113
Advance Access publication March 22, 2006

Original Contribution

Physical Activity, Insulin Sensitivity, and Hypertension among US Adults: Findings from the Insulin Resistance Atherosclerosis Study

Capri Gabrielle Foy[1], Kristie Long Foley[1], Ralph B. D'Agostino, Jr.[1], David C. Goff, Jr.[1], Elizabeth Mayer-Davis[2], and Lynne E. Wagenknecht[1]

[1] Department of Public Health Sciences, School of Medicine, Wake Forest University, Winston-Salem, NC.
[2] Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC.

Received for publication August 15, 2005; accepted for publication December 21, 2005.

Although regular physical activity is associated with less hypertension and improved insulin sensitivity, there is debate regarding the role of insulin sensitivity in hypertension. Thus, in this cross-sectional study, the authors investigated whether physical activity and insulin sensitivity were associated with hypertension. The sample consisted of 1,599 persons aged 40–69 years who participated in the Insulin Resistance Atherosclerosis Study. The outcome measure was hypertension as measured by a standard protocol. Energy expended in vigorous physical activity was calculated from a recall interview on past-year physical activity. Descriptive statistics revealed that 590 (37%) participants had prevalent hypertension. In adjusted logistic regression analysis, participants expending ≥150 kcal/day in vigorous physical activity had an odds ratio for hypertension of 0.73 (95% confidence interval (CI): 0.55, 0.98) in comparison with participants who were sedentary. Further adjustment for insulin sensitivity resulted in attenuation of the effect of vigorous physical activity on hypertension (odds ratio = 0.97, 95% CI: 0.71, 1.33), while the effect of insulin sensitivity was significant (odds ratio = 0.33, 95% CI: 0.26, 0.41). These results suggest that longitudinal studies are warranted to determine whether insulin sensitivity is a mediator of the relation between physical activity and hypertension.

adult; aged; exercise; hypertension; insulin; insulin resistance

Abbreviations: ACSM, American College of Sports Medicine; IRAS, Insulin Resistance Atherosclerosis Study; MET, metabolic equivalent; OR, odds ratio.

Insulin resistance has been implicated in the progression of cardiovascular disease (1) and the metabolic syndrome (2). It has also been associated with components of the metabolic syndrome, such as a high triglyceride level (3), a low high density lipoprotein cholesterol level, and central adiposity (4). However, the possible association between insulin resistance and hypertension, another component of the metabolic syndrome, has stimulated considerable debate (5). While early studies yielded equivocal results (6–10), more recent research has found that insulin resistance is linked to several components of blood pressure regulation, such as salt sensitivity (11), response of blood pressure to acute exercise (12), and left ventricular mass (13). Goff et al. (5) studied the relation between insulin resistance and 5-year incidence of hypertension among 840 normotensive participants in the Insulin Resistance Atherosclerosis Study (IRAS). After adjustment for age, gender, ethnicity, and smoking status, for each unit of increased insulin sensitivity (i.e., lower insulin resistance), the risk of hypertension was 10 percent lower.

One factor that may influence the effect of insulin resistance on hypertension is physical activity. For example, physical activity has been shown to be associated with more favorable insulin sensitivity in controlled studies (14, 15). In

Correspondence to Dr. Capri G. Foy, Department of Public Health Sciences, Wake Forest University School of Medicine, 2000 West First Street, Office 250, Winston-Salem, NC 27104 (e-mail: cfoy@wfubmc.edu).

an epidemiologic study, Mayer-Davis et al. (16), studying 1,467 IRAS participants, found that persons who reported engaging in vigorous activity five or more times per week had significantly greater insulin sensitivity than persons who rarely or never participated in vigorous physical activity.

Regular physical activity has also been shown to be associated with lower blood pressure among persons with hypertension in several early prospective studies (17, 18). In a recent study, Hayashi et al. (19), studying 6,017 Japanese men, found that the duration of the men's walk to work was significantly associated with a reduced risk of incident hypertension, suggesting a dose-response effect. Position statements issued by the American College of Sports Medicine (ACSM) and the Centers for Disease Control and Prevention recommend 30 continuous or total minutes of at least moderate-intensity physical activity on most, if not all, days of the week, regardless of hypertension status (20, 21).

Relatively few studies have investigated the relation between physical activity, hypertension, and insulin resistance. If regular physical activity does indeed reduce the prevalence of hypertension, one possible mechanism may be a favorable alteration of insulin resistance. Hence, our purpose in the present investigation was to examine whether insulin resistance was associated with the effect of vigorous or moderate physical activity on baseline blood pressure among adults enrolled in a cohort study. The large, multiethnic sample permitted us to consider the effects of age, gender, and ethnicity in this cross-sectional baseline examination.

MATERIALS AND METHODS

Overview of study design

IRAS was a large epidemiologic study designed to investigate the cross-sectional and prospective relations between insulin resistance, cardiovascular disease risk factors, and clinical and subclinical indicators of cardiovascular disease in a large, multiethnic population of US adults. IRAS was conducted at four clinical centers. African Americans and non-Hispanic Caucasian Americans were recruited from members of nonprofit health maintenance organizations in Oakland and Los Angeles, California. Hispanic Americans and non-Hispanic Caucasian Americans were studied at centers in the San Luis Valley of Colorado and San Antonio, Texas. The participants in Colorado and Texas were recruited from ongoing population-based epidemiologic studies investigating cardiovascular disease risk factors and type 2 diabetes among non-Hispanic Caucasian Americans and Hispanic Americans, specifically the San Luis Valley Diabetes Study and the San Antonio Heart Study. Sampling strategies were designed to identify persons of different age, ethnicity, gender, and glucose tolerance categories for the performance of within- and between-group analyses (22).

Participants

Participants in IRAS were community-dwelling adults aged 40–69 years. Exclusion criteria included the following: 1) treatment with corticosteroids within the past 6 months; 2) insulin treatment within the past 5 years; 3) severe limitation of caloric intake (<800 kcal/day); 4) decompensated congestive heart failure; 5) decompensated emphysema or chronic lung disease; 6) unstable angina; 7) active treatment for cancer; 8) breast cancer treated with surgery or radiation; 9) seizure disorder or epilepsy; 10) kidney dialysis, transplant, or renal failure; 11) serious illness within the past month (e.g., heart attack, major surgery); 12) pregnancy; or 13) cognitive or psychological dysfunction (22). Because of missing physical activity values, 25 observations were excluded, leaving 1,599 observations in the unadjusted analyses.

Baseline examination

The baseline clinical examination was performed in 1992–1993 and consisted of two 4-hour visits scheduled 1 week apart. Before each visit, participants were asked to refrain from alcohol intake and heavy physical exercise for 24 hours, to abstain from food for 12 hours, and to refrain from smoking on the day of the examination. Persons with diabetes who were using oral hypoglycemic agents were asked to not take their morning dose but bring it to the clinic.

The first visit included a 75-g oral glucose tolerance test, during which blood was collected for fasting and 2-hour glucose samples. Glucose tolerance status was classified according to World Health Organization criteria (23) as normal glucose tolerance, impaired glucose tolerance, or diabetes.

Variables

Outcome variable. Resting blood pressure was measured three times using a mercury manometer, after a 5-minute rest. The mean of the last two measurements was used to calculate baseline blood pressure. For this analysis, we dichotomized the continuous variables of systolic and diastolic blood pressure and the categorical variable of current blood-pressure medication use (yes/no) into a new categorical variable denoting hypertension (yes/no). Hypertension was defined as the presence of one of the following: systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg, or current pharmaceutical treatment for hypertension (24).

Independent variables. Energy expenditure during vigorous physical activity over the past year was determined via a 1-year recall of physical activity directed by centrally trained and certified interviewers (16). During the physical activity recall, the interviewer administered a modified version of a validated instrument that measured physical activities common among IRAS participants, including ranching-related and homemaking activities. Participants were queried about these activities in groups, according to the type of activity (home, work, or leisure time) and the intensity of the activity, which was based on published metabolic equivalent (MET) values. METs were defined as the ratio of the metabolic rate during an activity to the resting metabolic rate of 3.5 ml of oxygen/kg/minute (1 MET) (25). For each activity, usual frequency and duration of participation were recorded; from this, estimated energy expenditure was determined and expressed as kcal/kg/year, which we converted to kcal/day. Vigorous estimated energy expenditure (hereafter termed "vigorous physical activity") was defined as activity that carried a MET assignment of ≥6.0, while moderate estimated energy expenditure (hereafter termed "moderate physical activity") had a MET assignment of 3.5–5.9. Notably, 501 persons (31.3 percent) reported expending no energy in vigorous physical activity. Vigorous physical activity was further categorized into the following groupings: 0 kcal/day (sedentary), 1–149 kcal/day (underactive), or ≥150 kcal/day (meeting ACSM recommendations). Because of the small number of participants reporting no moderate activity ($n = 21$), the following groupings were used for moderate physical activity: ≤149 kcal/day (sedentary/underactive) and ≥150 kcal/day (meeting ACSM recommendations).

Insulin sensitivity was assessed by means of the frequently sampled intravenous glucose tolerance test with minimal model analyses. The insulin-modified protocol with 12 time points that is used in IRAS has been compared with the hyperinsulinemic-euglycemic clamp and has been shown to be a valid measure of insulin resistance, with a correlation with clamp measures of approximately 0.6, albeit with values approximately 50 percent lower than clamp values when expressed in the same units. Approximately 15.6 percent of the sample had an insulin sensitivity value of 0. Therefore, we performed the following calculation for each participant (16): ln(insulin sensitivity + 1).

Demographic and clinical variables. Information regarding age, gender, ethnicity, parental history of hypertension, smoking status (never, former, or current), usual alcohol intake, and medication use was obtained through self-report. Clinic site was determined by study staff. Waist circumference was measured in duplicate on bare skin in midrespiration, using steel tape at the natural indentation between the 10th rib and the iliac crest, to the nearest 0.5 cm. Current usual consumption of alcohol over the previous month was estimated using a 10-item questionnaire from which overall alcohol intake in grams per day was calculated (26).

Statistical analyses

For descriptive purposes, we generated preliminary summary statistics for the sample to determine the characteristics of persons in each category of vigorous physical activity over the past year. To determine whether there were differences between the categories, we conducted one-way analyses of variance on the continuous variables and Pearson χ^2 tests on categorical variables.

The relation between physical activity, insulin sensitivity, and hypertension was examined through logistic regression in four separate models. The first analysis tested the effect of vigorous physical activity on the presence of hypertension in an unadjusted model. Adjusted model 1 tested the effect of vigorous physical activity on hypertension in a model with seven covariates (age, gender, ethnicity, parental history, smoking status, alcohol intake, and clinic) and an ethnicity × site interaction term. Adjusted model 2 included the above covariates, with the addition of insulin sensitivity for determination of whether its inclusion attenuated the effect of physical activity compared with adjusted model 1. In addition, because adiposity may be a causal antecedent to impaired insulin sensitivity (4, 7), in adjusted model 3 we added waist circumference as a covariate to determine whether its inclusion attenuated the effect of insulin sensitivity. Identical procedures were used to determine the relations between moderate physical activity, insulin sensitivity, and hypertension. Because the amount of vigorous physical activity may obscure the effect of moderate physical activity on hypertension, we conducted identical analyses of moderate physical activity that were restricted to the 501 participants who reported expending no energy in vigorous physical activity.

Interestingly, our original analysis plan involved testing a priori hypotheses regarding the effect of three-way interactions between physical activity, ethnicity, and insulin sensitivity on hypertension, adjusted for the covariates listed above. However, these interactions were not significant, and thus these results are not presented. In addition, our original analysis plan entailed testing the effect of frequency of vigorous physical activity on hypertension, using the following categories of vigorous physical activity: never or rarely engaged in (reference category), 1–3 times per month, once per week, 2–4 times per week, and five or more times per week. The results in these models were similar to those found when we tested the effect of categories of kilocalorie expenditure in vigorous physical activity and thus are not presented.

The alpha level for testing the significance of effects in each model was set a priori at $p < 0.05$. All analyses were conducted using the Statistical Package for the Social Sciences, version 10.10 (SPSS, Inc., Chicago, Illinois).

RESULTS

Total sample

As noted above, because of missing physical activity values, 25 observations were excluded, leaving 1,599 observations in the unadjusted analyses. Descriptive data for each of the vigorous physical activity categories (in kcal/day) are shown in table 1, and the participants' covariate characteristics at baseline are shown in table 2, partitioned by category of physical activity over the previous year. Persons in the higher categories of vigorous physical activity were predominately male, Caucasian, and younger, had greater mean insulin sensitivity, consumed more alcohol, and had less prevalence of hypertension.

Physical activity

Vigorous physical activity. Table 3 shows results from the unadjusted and adjusted models for the prevalence of hypertension according to category of vigorous physical activity. In the unadjusted model, participants in the 1–149 kcal/day category demonstrated lower odds of hypertension than participants with no vigorous activity (odds ratio (OR) = 0.69, $p = 0.003$). Participants expending ≥150 kcal/day had significantly lower odds of hypertension than participants with no vigorous physical activity (OR = 0.57, $p < 0.001$). In

TABLE 1. Amount of energy expended per day (kcal/day) in vigorous physical activity, by category of vigorous physical activity, Insulin Resistance Atherosclerosis Study, 1992–1993

	Category of vigorous physical activity		
	Sedentary (0 kcal/day) ($n = 501$)	Underactive (1–149 kcal/day) ($n = 527$)	Recommended (≥150 kcal/day) ($n = 571$)
Mean	0.00	54.85	707.02
Standard deviation	0.00	41.02	811.63
Median	0.00	49.45	416.22
Interquartile range			
25th percentile	0.00	16.94	251.43
75th percentile	0.00	85.59	780.96

adjusted model 1, participants in the ≥150-kcal/day category had significantly lower odds of hypertension than participants with no vigorous physical activity (OR = 0.73, $p = 0.04$). Missing values for insulin sensitivity ($n = 128$) reduced the sample size to 1,471 observations in adjusted model 2. After additional adjustment for insulin sensitivity in adjusted model 2, the odds ratios for the categories of vigorous physical activity energy expenditure were no longer significant; however, increased insulin sensitivity was associated with significantly lower odds of hypertension (OR = 0.33, $p < 0.001$). Finally, after further adjustment for waist circumference in adjusted model 3, the odds ratios for categories of vigorous physical activity energy expenditure remained nonsignificant, with waist circumference and insulin

TABLE 2. Characteristics of participants by category of vigorous physical activity at baseline, Insulin Resistance Atherosclerosis Study, 1992–1993

Variable	Category of vigorous physical activity						*p* value
	Sedentary (0 kcal/day) ($n = 501$)		Underactive (1–149 kcal/day) ($n = 527$)		Recommended (≥150 kcal/day) ($n = 571$)		
	Mean or no.	SD* or %	Mean or no.	SD or %	Mean or no.	SD or %	
Mean and SD							
Age (years)	57.78	8.19	55.64	8.26	53.84	8.51	<0.001
Ln(insulin sensitivity + 1) (10^{-4}/minute/μU/ml)	0.67	0.53	0.82	0.61	0.86	0.57	<0.001
Waist circumference (cm)	94.56	14.79	91.72	13.72	94.10	11.82	0.001
Alcohol consumption (g/day)	3.98	11.18	6.27	14.44	8.02	15.34	<0.001
Number and percent							
Gender							
Female	367	73.3	321	60.9	199	34.9	<0.001
Male	134	26.7	206	39.1	372	65.1	
Ethnicity							
African-American	151	30.1	157	29.8	147	25.7	0.01
Caucasian-American	161	32.1	204	38.7	238	41.7	
Hispanic-American	189	37.7	166	31.5	186	32.6	
Glucose tolerance							
Normal	176	35.1	244	46.3	289	50.6	<0.001
Impaired	131	26.1	109	20.7	120	21.0	
Diabetes	194	38.7	174	33.0	162	28.4	
Smoking status							
Never	230	45.9	242	45.9	226	39.6	0.11
Former	185	36.9	197	37.4	250	43.8	
Current	86	17.2	88	16.7	95	16.6	
Blood pressure							
Normal	278	55.5	340	64.5	391	68.5	<0.001
Hypertension	223	44.5	187	35.5	180	31.5	
Parental history of hypertension							
No	263	52.5	267	50.7	274	48.0	0.33
Yes	238	47.5	260	49.3	297	52.0	

* SD, standard deviation.

TABLE 3. Unadjusted and adjusted odds ratios† for the presence of hypertension according to physical activity, insulin sensitivity, and waist circumference, Insulin Resistance Atherosclerosis Study, 1992–1993

	No. of participants	Unadjusted		Adjusted model 1‡		Adjusted model 2§		Adjusted model 3¶	
		OR#	95% CI#	OR	95% CI	OR	95% CI	OR	95% CI
Vigorous physical activity									
Category of vigorous physical activity		(*n* = 1,599)		(*n* = 1,599)		(*n* = 1,471)		(*n* = 1,469)	
Sedentary (0 kcal/day)	501	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Underactive (1–149 kcal/day)	527	0.69**	0.53, 0.88	0.82	0.62, 1.09	1.03	0.75, 1.39	1.05	0.77, 1.43
Recommended (≥150 kcal/day)	571	0.57***	0.45, 0.74	0.73*	0.55, 0.98	0.97	0.71, 1.33	0.98	0.71, 1.36
Insulin sensitivity						0.33***	0.26, 0.41	0.47***	0.36, 0.61
Waist circumference								1.03***	1.02, 1.04
Moderate physical activity									
Category of moderate physical activity		(*n* = 495)		(*n* = 495)		(*n* = 443)		(*n* = 442)	
Sedentary/underactive (0–149 kcal/day)	126	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Recommended (≥150 kcal/day)	369	1.28	0.85, 1.94	1.22	0.77, 1.92	1.54	0.91, 2.59	1.49	0.87, 2.53
Insulin sensitivity						0.34***	0.22, 0.52	0.44***	0.26, 0.74
Waist circumference								1.02*	1.00, 1.04

* $p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

† Obtained from logistic regression analysis.

‡ Results were adjusted for age, gender, smoking status, alcohol intake, parental history of hypertension, ethnicity, clinic, and ethnicity × clinic and were rounded to the nearest 0.01.

§ Results were adjusted for age, gender, smoking status, alcohol intake, parental history of hypertension, ethnicity, clinic, insulin sensitivity, and ethnicity × clinic and were rounded to the nearest 0.01.

¶ Results were adjusted for age, gender, smoking status, alcohol intake, parental history of hypertension, ethnicity, clinic, insulin sensitivity, waist circumference, and ethnicity × clinic and were rounded to the nearest 0.01.

OR, odds ratio; CI, confidence interval.

sensitivity both being significantly associated with hypertension (OR = 1.03 ($p < 0.001$) and OR = 0.47 ($p < 0.001$), respectively).

Moderate physical activity. Table 3 also displays results from unadjusted and adjusted models for the effect of energy expenditure in moderate physical activity on hypertension among the 501 participants who reported no vigorous physical activity. In the unadjusted model and the three adjusted models, participants in the ≥150-kcal/day category did not exhibit significantly different odds of hypertension than participants in the 0–149-kcal/day category. In adjusted model 2, insulin sensitivity was associated with lower odds of hypertension (OR = 0.34, $p < 0.001$). In adjusted model 3, waist circumference was associated with increased odds of hypertension (OR = 1.02, $p < 0.01$), while insulin sensitivity was associated with lower odds (OR = 0.44, $p < 0.001$).

Among covariates for the prevalence of hypertension in the adjusted models for vigorous and moderate physical activity, age, African-American ethnicity, parental history of hypertension, and alcohol consumption were consistently associated with significantly increased odds of hypertension across models. Conversely, Hispanic Americans and current smokers had significantly lower odds of hypertension across all models. With the exception of adjusted model 3, there were no significant differences in the odds of hypertension by gender, and former smokers did not have significantly different odds of hypertension than participants who had never smoked. Interestingly, in all three models, smokers evidenced lower odds of hypertension than never smokers. Similar trends were observed for moderate physical activity in the subset of participants who reported no vigorous physical activity.

DISCUSSION

This study was designed to investigate the effects of physical activity and insulin sensitivity on hypertension in a cross-sectional, multiethnic sample of older adults. To our knowledge, this is the first study to have examined the effect of insulin sensitivity in this relation using direct measurement instead of surrogate measures. Collectively, our results suggest that participants who meet or exceed current caloric expenditure recommendations for vigorous physical activity demonstrate significantly less hypertension than do sedentary or underactive participants. The results also accentuate the finding that insulin sensitivity was associated with the relation between vigorous physical activity and hypertension among participants with normal glucose tolerance, as well as in our total sample. Indeed, the addition of insulin sensitivity in the logistic regression models appreciably attenuated the effect of physical activity on hypertension. To our knowledge, this is the first study to report this direct association between physical activity, insulin sensitivity, and hypertension in a cross-sectional sample of older adults.

Several of our findings are consistent with those of other investigators (27, 28). For instance, Whelton et al. (27) conducted a meta-analysis of 54 randomized clinical trials that examined the effect of aerobic exercise on blood pressure. Using a random-effects model in which data from each trial were pooled and weighted by the inverse of the total variance, the authors found that aerobic exercise was associated with a significant reduction in both mean systolic blood pressure and mean diastolic blood pressure. The authors found that this relation existed among both normotensive and hypertensive participants, as well as among overweight and normal-weight persons. Our results are also consistent with those of Mayer-Davis et al. (16), who studied the relation between physical activity and insulin sensitivity among 1,467 IRAS participants. In linear regression analyses investigating the effect of physical activity on insulin sensitivity, adjustment for potential confounders showed that increased participation in vigorous physical activity was associated with significant increases in insulin sensitivity (16).

It is puzzling that participants meeting caloric expenditure recommendations for moderate physical activity did not have significantly less hypertension than persons who were sedentary or underactive in any of the adjusted models. This result is inconsistent with the summary findings of the Whelton et al. (27) and Fagard (28) meta-analyses, which found that the reductions in blood pressure were similar among trials involving high-intensity exercise and those involving moderate-intensity exercise. The recently published ACSM Position Stand on exercise and hypertension (21) also concludes from the existing evidence that moderate-intensity exercise confers similar benefits on blood pressure as high-intensity exercise, while reducing the risk of cardiovascular complications, orthopedic injuries, and nonadherence. Indeed, we found that 38.9 percent of participants in the $\geq$150-kcal/day moderate physical activity category were also in the $\geq$150-kcal/day vigorous physical activity category. We performed analyses of moderate physical activity that were restricted to participants reporting no vigorous physical activity; they failed to yield significant effects. It is possible that our analyses did not include other relevant covariates (i.e., confounders) that obscured the relation between moderate physical activity and hypertension among these participants.

Our findings prompt us to speculate regarding several possible mechanisms by which physical activity may influence hypertension that were beyond the scope of this investigation. For instance, several cross-sectional studies have found that physical activity produces structural adaptations in the vasculature, such as increased lumen diameter (29, 30). Dinenno et al. (31) found that among 22 men who engaged in 3 months of aerobic leg exercise, lumen diameter was significantly increased, while intima-media thickness and the ratio of intima-media thickness to lumen diameter were decreased. Pescatello et al. (21) speculated that regular physical activity may result in reduced sympathetic nervous system activity and norepinephrine release, which in turn may cause reductions in vasoconstriction and total peripheral resistance. Meredith et al. (32) found that reductions in norepinephrine after training were associated with decreased spillover, suggesting that sympathetic nervous system activity was decreased. Other researchers (33, 34) have found that nitric oxide production, which influences endothelial cell-dependent vasodilation, is increased through exercise training.

These cross-sectional findings encourage further investigation regarding increased insulin sensitivity as a possible pathway by which physical activity influences blood pressure. Although several previous studies have established an association between physical activity and insulin sensitivity, the mechanisms by which physical activity favorably influences insulin sensitivity remain unclear (35). Perseghin et al. (36) proposed that vigorous physical activity may lead to reductions in fasting insulin levels and increased insulin sensitivity through enhanced glucose transport, which replenishes glycogen stores. Along with decreases in fat mass, physical activity may also result in an increase in fat-free mass, which in turn increases the volume of muscle tissue available for glucose transport.

In addition, the mechanisms by which insulin sensitivity may modify hypertension are yet to be fully explored. For instance, our findings suggest that the effect of insulin sensitivity on blood pressure may be associated, in part, with waist circumference. Blood pressure involves the interplay between complex arrays of neural, hormonal, and mechanical systems, all of which may be affected by insulin sensitivity (37). For instance, Cruz et al. (37) postulated that poor insulin sensitivity may lead to impaired endothelial cell function, increases in sympathetic nervous system activity, and renal sodium reabsorption. Landsberg (38) hypothesized that insulin resistance is associated with decreased muscle glucose intake and increased sympathetic nervous system activity, both of which contribute to increases in blood pressure. This cross-sectional investigation prohibits us from inferring causal relations; only prospective trials with a priori questions would be able to fully elucidate the relations between physical activity, insulin sensitivity, and hypertension.

This study had several strengths, including direct assessment of insulin sensitivity as opposed to use of surrogate measures. IRAS included nearly equal representation of older African Americans, Hispanic Americans, and Caucasian Americans and men and women from multiple testing sites, which enhances the external validity of our findings. In addition, several relevant demographic and health status variables were considered as possible confounding factors in our logistic regression models. In this investigation, we relied on self-reported physical activity, which is common in observational studies in which physical activity is not an endpoint. The findings would have been strengthened through assessments that were beyond the scope of the original IRAS study, such as triangulation of measurements of physical activity and cardiorespiratory fitness via accelerometry or graded exercise tests. It is also important to note that persons who regularly engage in physical activity may be conscientious about engaging in other health-promoting behaviors that may positively affect blood pressure, such as following healthy eating patterns and complying with physicians' advice. Finally, the cross-sectional nature of this investigation prohibited us from determining temporal relations among physical activity, insulin sensitivity, and hypertension.

In conclusion, these results enhance our understanding of insulin sensitivity as a possible mechanism through which physical activity protects against hypertension, and they add support to current recommendations regarding interventions that improve insulin sensitivity and blood pressure. In future prospective studies and randomized clinical trials, researchers should further investigate the specific mechanisms by which physical activity influences insulin sensitivity, as well as the means by which insulin sensitivity affects hypertension.

ACKNOWLEDGMENTS

This research was supported by the National Heart, Lung, and Blood Institute (grants HL47887, LH47889, HL47890, HL47892, and HL47902) and by the General Clinical Research Centers Program of the National Center for Research Resources, National Institutes of Health (grants M01 RR431 and M01 RR01346). Dr. Capri G. Foy was partially supported by the Claude D. Pepper Older Americans Independence Center, Wake Forest University (grant P30-AG21332).

Conflict of interest: none declared.

REFERENCES

1. Zimmet P, Boyko EJ, Collier GR, et al. Etiology of the metabolic syndrome: potential role of insulin resistance, leptin resistance, and other players. Ann N Y Acad Sci 1999;892:25–44.
2. Reaven G. Metabolic syndrome: pathophysiology and implications for management of cardiovascular disease. Circulation 2002;16:286–8.
3. Grundy SM. Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. Am J Cardiol 1999;83:25F–9F.
4. Thomas GN, Hong AW, Lam CW, et al. Increasing insulin resistance contributes to worsening glycaemic and lipid profiles in older Chinese subjects. Diabetes Res Clin Pract 2004;64:123–8.
5. Goff DC Jr, Zaccaro DJ, Haffner SM, et al. Insulin sensitivity and the risk of incident hypertension: insights from the Insulin Resistance Atherosclerosis Study. Diabetes Care 2003;26:805.
6. Muller DC, Elahi D, Pratley RE, et al. An epidemiological test of the hyperinsulinemia-hypertension hypothesis. J Clin Endocrinol Metab 1993;76:544–8.
7. Haffner SM, D'Agostino RB Jr, Saad MF, et al. Increased insulin resistance and insulin secretion in nondiabetic African-Americans and Hispanics compared with non-Hispanic whites. The Insulin Resistance Atherosclerosis Study. Diabetes 1996;45:742–8.
8. Haffner SM. Insulin and blood pressure: fact or fantasy? J Clin Endocrinol Metab 1993;76:541–3.
9. Snorgaard O, Kober L, Carlsen J. The effect of metformin on blood pressure and metabolism in nondiabetic hypertensive patients. J Intern Med 1998;242:407–12.
10. Reaven GM. Insulin resistance may or may not play a role in blood pressure regulation. J Intern Med 1998;244:359–60.
11. Suzuki M, Kimura Y, Tsushima M, et al. Association of insulin resistance with salt sensitivity and nocturnal fall of blood pressure. Hypertension 2000;35:864–8.
12. Brett SE, Ritter JM, Chowienczyk PJ. Diastolic blood pressure changes during exercise positively correlate with serum cholesterol and insulin resistance. Circulation 2000;101:611–15.
13. Phillips RA, Krakoff LR, Dunaif A, et al. Relation among left ventricular mass, insulin resistance, and blood pressure in nonobese subjects. J Clin Endocrinol Metab 1998;83:4284–8.
14. Houmard JA, Tanner CJ, Slentz CA, et al. Effect of the volume and intensity of exercise training on insulin sensitivity. J Appl Physiol 2004;96:101–6.
15. Holloszy JO, Schultz J, Kusnierkiewicz J, et al. Effects of exercise on glucose tolerance and insulin resistance. Brief review and some preliminary results. Acta Med Scand Suppl 1986;711:55–65.
16. Mayer-Davis EJ, D'Agostino R Jr, Karter AJ, et al. Intensity and amount of physical activity in relation to insulin sensitivity: The Insulin Resistance Atherosclerosis Study. JAMA 1998;279:669–74.
17. Paffenbarger RS Jr, Wing AL, Hyde RT, et al. Physical activity and incidence of hypertension in college alumni. Am J Epidemiol 1983;117:245–57.
18. Paffenbarger RS Jr, Jung DL, Leung RW, et al. Physical activity and hypertension: an epidemiological view. Ann Med 1991;23:319–27.
19. Hayashi T, Tsumura K, Suematsu C, et al. Walking to work and the risk for hypertension in men: The Osaka Health Survey. Ann Intern Med 1999;131:21–6.
20. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA 1995;273:402–7.
21. Pescatello LS, Franklin BA, Fagard R, et al. American College of Sports Medicine Position Stand. Exercise and hypertension. Med Sci Sports Exerc 2004;36:533–53.
22. Wagenknecht LE, Mayer EJ, Rewers M, et al. The Insulin Resistance Atherosclerosis Study (IRAS): objectives, design, and recruitment results. Ann Epidemiol 1995;5:464–72.
23. World Health Organization. Diabetes mellitus: report of a WHO study group. Geneva, Switzerland: World Health Organization, 1985. (WHO Technical Report Series no. 727).
24. Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. JAMA 2003;289:2560–72.
25. Ainsworth BE, Haskell WL, Leon AS, et al. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 1993;25:71–80.
26. Bell RA, D'Agostino RB Jr, Mayer-Davis EJ, et al. Associations between alcohol consumption and insulin sensitivity and cardiovascular disease risk factors. Diabetes Care 2000;23:1630–6.
27. Whelton SP, Chin A, Xin X, et al. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med 2002;136:493–503.
28. Fagard RH. Exercise characteristics and the blood pressure response to dynamic physical training. Med Sci Sports Exerc 2001;33(suppl):S484–92.
29. Huonker M, Halle M, Keul J. Structural and functional adaptations of the cardiovascular system by training. Int J Sports Med 1996;17(suppl 3):S164–72.
30. Wijnen JA, Kuipers H, Kool MJ, et al. Vessel wall properties of large arteries in trained and sedentary subjects. Basic Res Cardiol 1991;86(suppl 1):25–9.

31. Dinenno FA, Tanaka H, Monahan KD, et al. Regular endurance exercise induces expansive arterial remodelling in the trained limbs of healthy men. J Physiol (Lond) 2001;534:287–95.
32. Meredith IT, Friberg P, Jennings L. Exercise training lowers resting renal but not cardiac sympathetic activity in humans. Hypertension 1991;18:575–82.
33. Higashi Y, Sasaki S, Kurisu S. Regular aerobic exercise augments endothelium dependent vascular relaxation in normotensive as well as hypertensive subjects: role of endothelium-derived nitric oxide. Circulation 1999;100:1194–202.
34. Kingwell BA. Nitric oxide-mediated metabolic regulation during exercise: effects of training in health and cardiovascular disease. FASEB J 2000;14:1685–96.
35. Schmitz KH, Jacobs DR, Hong C-P, et al. Association of physical activity with insulin sensitivity in children. Int J Obes 2002;26:1310–16.
36. Perseghin G, Price TB, Petersen KF, et al. Increased glucose transport-phosphorylation and muscle glycogen synthesis after exercise training in insulin-resistant subjects. N Engl J Med 1996;335:1357–62.
37. Cruz ML, Huang TT, Johnson MS, et al. Insulin sensitivity and blood pressure in black and white children. Hypertension 2002;40:18–22.
38. Landsberg L. Insulin-mediated sympathetic stimulation: role in the pathogenesis of obesity-related hypertension (or how insulin affects blood pressure, and why). J Hypertens 2001;19:523–8.