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Risk Factors for Prehypertension in the Community: A prospective analysis from the Western New York Health Study

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Abstract

Prehypertension is an increasingly highly prevalent condition in the general population, and is associated with an increased risk for coronary heart disease and stroke. However, evidence from population-based studies of the risk factors for prehypertension is scant. We sought to examine the predictors of progression from normotension to prehypertension in a community-based population from Western New York.

A longitudinal analysis, over 6 years of follow-up, among 569 men and women (mean age 51.8 years) who were free of prehypertension, hypertension, cardiovascular disease and diabetes at the baseline examination, in the Western New York Health Study (WNYHS). Incident prehypertension at follow-up was defined as systolic blood pressure of 120–139 mmHg and/or diastolic blood pressure of 80–89 mmHg.

The cumulative six year incidence of prehypertension was 33.5% (189/564). In bivariate analyses, there were several correlates of incident prehypertension, including age, BMI and waist circumference, impaired fasting glucose (IFG), uric acid, and baseline blood pressure levels. After multivariate adjustment, IFG at baseline [odds ratio (OR): 1.70, 95%CI: 1.07–2.69) and weight gain since age 25 (OR: 1.12, 1.04–1.21 per 10 lb increase) were the strongest significant predictors of prehypertension at follow-up. Neither baseline waist circumference nor change in BMI were predictor variables in models when they were substituted for weight gain.

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Disclosures
None

Results from this study suggest early dysregulation of glucose metabolism and weight gain over the lifespan may represent important risk factors for prehypertension in the general population.

Keywords

blood pressure; metabolic syndrome; prehypertension; prospective; risk factors; weight change

Introduction

Prehypertension, defined as the blood pressure range of 120 to 139 mm Hg systolic or 80 to 89 diastolic is present in approximately 70 million Americans (1, 2). This condition is a risk factor for coronary heart disease, frank hypertension, and stroke (3). Current preventive approaches to prehypertension are not entirely effective in controlling this condition and many prehypertensive subjects will progress to have hypertension (4).

Prospective population-based studies of the risk factors for prehypertension or its sequels are scant (5–7). For example, the Framingham Heart Study (5) reported a risk factor-adjusted hazard ratio for cardiovascular disease (CVD) of 2.5 for women and 1.6 for men with high normal blood pressure (systolic blood pressure of 130 to 130 mmHg, diastolic pressure 80 to 89 mmHg or both) relative to those with optimal blood pressure. The Strong Heart Study (6) showed that many prehypertensive persons would progress to have hypertension over four years and could be identified by echocardiographic findings at baseline as well as metabolic variables including diabetes. Data from the Women's Health Initiative (7) indicate that prehypertension is a common condition in postmenopausal women and is associated with an increased risk of all manifestations of CVD.

Prehypertension is often associated with the metabolic syndrome consisting in part of obesity, insulin resistance and elevated blood pressure and it is unclear whether prehypertension alone or the other related risk factors is more important in determining the optimal preventive strategy. We sought to examine the predictors of progression from normotension to prehypertension in a community-based population derived from Erie and Niagara Counties in Western New York. Precursors to prehypertension were examined over six years of follow-up in over 500 men and women who were initially free of prehypertension, hypertension, cardiovascular disease and diabetes in the Western New York Health Study (WNYHS). We hypothesized that metabolic and cardiovascular risk factors would predict incident prehypertension among normotensive middle- aged and older participants from the WNYHS.

Methods

Study Population

Details of the WNYHS have been previously published (8–10). Participants were originally enrolled as healthy subjects (i.e., without clinically evident cardiovascular disease) in the Western New York Health Study, an epidemiologic case-control investigation of patterns of alcohol intake and coronary heart disease in Erie and Niagara Counties, New York conducted from 1996–2001 (59.5% response rate). The cohort was selected from drivers' license lists and Health Care Finance Administration lists. Eligible participants for the follow-up examination were men and women aged 35–79 years selected from the baseline examination without known CVD or type 2 diabetes defined by a fasting glucose > 125 mg/dl or receipt of oral hypoglycemic medication and who were capable of completing the study protocol (n = 2652). Exclusion criteria included: self report of any medical condition that would prohibit participation (e.g., all cancers except skin cancer, type 1 diabetes,

physical or mental impairment, or inability to contact and determine eligibility). This left 2139 persons eligible for the follow-up visit in 2003–2004 of whom 1455 attended our clinic (68% response rate). The protocol was approved by the Buffalo Health Science Institutional Review Board and all participants provided written informed consent.

Incident prehypertension was assessed at the time of the follow-up clinic examination from 2003–2004 (follow-up of 5.9 +/− 0.8 years). For the purpose of this report, we selected participants who were normotensive at baseline who also participated in the follow-up reexamination. Prehypertension at follow-up was defined according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) guidelines (systolic BP of 120–139 mm Hg and/or diastolic BP of 80–89 mm Hg (1). Exclusion criteria included: type 2 diabetes mellitus at baseline, baseline use of antihypertensive medications or hypertension (defined as systolic >= 140 mm Hg, and/or diastolic BP >= 90 mm Hg) or hypertension at the follow-up examination. This left 564 eligible normotensive participants available for these analyses.

Clinical Examination and Classification of Participants

At both the baseline and follow-up visits, participants underwent a clinical examination that included resting blood pressure. Three consecutive measurements of systolic and diastolic blood pressure (first and fifth Korotkoff sounds) were performed with an appropriately sized cuff using a Baum mercury sphygmomanometer (WA Baum Co) after the participant had been seated for 5 minutes. The mean of the second and third reading were used in the analyses. Questionnaires that were first administered at the baseline visit were re-administered at the follow-up visit. These assessed lifestyle and health habit information including: cigarette use, physical activity, alcohol use, general health and well-being, sleep habits, personal and family history of diseases, medication use, and socioeconomic status. Physical activity was assessed with the Stanford 7-Day Recall questionnaire (11) which has been shown to have excellent validity in epidemiologic studies (12). The questionnaire was interviewer-administered at the baseline clinic visit. Participants were asked to recall (to the nearest half hour) time spent sleeping and in moderate, hard and very hard activities (either sports/recreational or household) in the previous 7 days. They were provided cards with examples of activities at each intensity level to help them estimate the absolute intensity of their activities. For the current report, we created several variables to examine physical activity: 1) a dichotomous variable characterizing participants as having no vs. any activity within each type of activity and for all activities combined; 2) duration of activity based upon hours/week; and 3) intensity of activity categorized as participation in moderate only and moderate plus hard, and very hard activity; and 3) total volume of activity in MET-hours/week – calculated by multiplying the time in hours by the MET level of the reported activity. One MET is approximately equivalent to sitting quietly. This latter variable was used in our analyses. We also queried about the amount of weight change since age 25.

Anthropometric measurements were performed including the waist circumference (mean of 2 measures taken at the mid-point of the ileac crest and the bottom of the last rib) as an index of central adiposity, and body mass index expressed as weight in kilograms (kg)/ height in meters (m) squared. Fasting glucose was measured after an overnight fast and determined using the glucose oxidase method (Beckman Instruments, Fullerton, CA). Diabetes and impaired fasting glucose were classified by 1997 American Diabetes Association guidelines (13). Quality control measures for BP measures included repeated measures and retraining of technicians if needed, direct observation by supervisors, and a manometer maintenance program.

Statistical Analysis

All data were analyzed using SPSS 18.0 (SPSS, Chicago, IL). Baseline characteristics between those that developed prehypertension and those that did not were compared by t-test for continuous variables or chi-square for categorical variables. Interaction was assessed with log-likelihood models, comparing the model with the interaction term to the model without the interaction term. There were no significant interactions noted thus age and gender were treated as covariates in the multivariate analyses. All of the variables associated with prehypertension at follow-up were entered into a forward stepwise logistic regression model (P to enter = 0.05; P to remove > = 0.1). The OR and 95% CI are presented for each model. All statistical tests were two sided and tests of alpha < 0.05 were considered statistically significant.

Results

Table 1 presents descriptive statistics of the study population. The mean age was approximately 52 years. The study sample tended to be female and overweight (mean BMI of 26.2) while the mean blood pressure was 106.8 mmHg systolic over 66.8 mmHg diastolic. Nearly twenty-five percent of the study sample had IFG.

Table 2 presents results of data stratified according to whether or not participants progressed to prehypertension or remained normotensive at follow-up. Those who progressed to prehypertension were significantly older at baseline, had a larger waist circumference and BMI, and higher systolic and diastolic blood pressures as well ($p<0.05$ for each). Leisure time physical activity did not differ significantly between the two groups (P = 0.283). IFG was more common among those who became prehypertensive over the follow-up period (34.9% vs. 19.7%; $p < 0.001$).

Uric acid was also higher among those who progressed ($p = 0.006$). Those who became prehypertensive had gained more weight since age 25 compared to those that remained normotensive (P = 0.005).

The results of the stepwise multiple logistic regression model are presented in table 3. After adjustment for age and baseline systolic blood pressure, IFG at baseline (OR 1.69, 95% CI: 1.06–2.67) and weight gain since age 25 (OR: 1.28, 95% CI: 1.11–1.58 per 10 lb increase) were statistically significant predictors of prehypertension at follow-up. Neither waist circumference nor current BMI were predictor variables in models when they were substituted for weight gain Change in BMI (not shown) was also not significant perhaps due to the relatively low mean change over the six years (Mean 0.788; SD 1.953). Other variables such as sleep duration, measures of general health status (SF-36), physical activity and uric acid were not significant predictors of prehypertension at follow-up in the multivariate model.

Discussion

The cumulative six-year incidence of prehypertension was 33.5 % in this cohort. Risk factor clustering with incident prehypertension was evident with higher baseline levels of body mass index, waist circumference, total METS (inversely), systolic and diastolic blood pressure, category of glucose tolerance, and uric acid higher among those who became prehypertensive. Those who reported significant weight gain since the age of 18 also were more likely to become hypertensive. However in multivariate results, only age, baseline systolic blood pressure, impaired fasting glucose and weight gain since age 25 were significantly associated with an increased risk of incident prehypertension in this community - wide sample of healthy individuals.

We found that weight gain through adulthood, the presence of IFG, along with age and baseline systolic blood pressure were important predictors of 6-year incident prehypertension, independent of other metabolic and lifestyle factors associated with prehypertension. Results from this study support the notion that early dysregulation of glucose metabolism and weight gain are likely to represent important risk factors for prehypertension in the general population.

The Shenghai Men's Study (14) and a similar cross-sectional report in Chinese women (15) demonstrated a linear relation between systolic blood pressure and weight gain since age 20. Among men, those in the highest quintile of weight gain since age 20 demonstrated a four-fold risk of developing prehypertension compared to those in the lowest quintile. The results among women were comparable.

The exact mechanism through which weight or body fat increases blood pressure is not entirely understood. However, obesity is closely related to insulin resistance and both may lie at the heart of the metabolic syndrome. We and others (16,17) have proposed that insulin resistance and compensatory hyperinsulinemia may play an important role in mediating the weight/blood pressure association. Hyperinsulinemia may raise blood pressure through multiple mechanisms including: enhanced activation of the SNS; increased sodium reabsorption, endothelial dysfunction; and up-regulation of the rennin-angiotensin system. However, because IFG also entered the stepwise regression and may itself be a marker for insulin resistance/hyperinsulinemia, other mechanisms must be at play. Fasting glucose concentrations are determined largely by the rate of hepatic glucose production which relates to hepatic rather than peripheral insulin resistance (18). Additionally, beta cell function has been reported to decline with increasing fasting glucose in the non-diabetic range (19). Thus, the inclusion of both weight gain since age 25 and IFG in the regression model may signal the presence of both insulin resistance as well as a loss of beta cell sensitivity as important pathways in the evolution of prehypertension. We had no direct assessment of beta cell function and thus could not directly test this hypothesis. The clustering of risk factors that we observed in bivariate analyses that were no longer significant upon multivariate analyses suggests that IFG and/or weight gain during adulthood are responsible for much of the variance in prehypertension that was due to these CVD risk factors. This would be consistent with the idea that insulin resistance as reflected by weight and IFG clusters with these other risk factors and that once insulin resistance or its proxies are entered into the regression model, the statistical significance of these other CVD risk factors is diminished or lost.

This report provides estimates of incidence of prehypertension and its precursors on a background of contemporary medical care in the community with careful attention paid to outcome assessment and uses the categories as defined by the JNC VII. Limitations to this study include the paucity of minority participants, thus our results may not be generalizable to nonwhite persons. Despite this limitation, participants were selected from a general population sample that is racially representative of the Western New York region.

In this community-based study of middle-aged and older adults we found that weight gain during adulthood and impaired fasting glucose were associated with the six-year risk of prehypertension. These results underscore the importance of weight management and further suggest that attention should be paid to maintaining normoglycemia to prevent prehypertension.

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Table 1

Characteristics of study participants (n=564)

Baseline characteristics	
Age (years), mean (SD)	51.8 (10.6)
Gender, n (%) Female	398 (70.6)
Race/Ethnicity, n (%) Caucasian	544 (96.5)
Smoking status, n (%)	
Never	297 (52.7)
Former	193 (34.3)
Current	73 (13.0)
Drinking status, n (%)	
Abstainer	49 (8.8)
Non-current (not in past 30 days)	116 (20.7)
Current	395 (70.5)
Waist circumference (cm), mean (SD)	84.7 (12.6)
Body mass index (kg/m^2), mean (SD)	26.2 (4.7)
MET-hrs from leisure time activity in the past 7 days, mean (SD)	28.0 (29.3
SBP mmHg mean (SD)	106.8 (7.7)
DBP mmHg mean (SD)	66.8 (6.6)
Glycemic status, n (%)	
NGT	424 (75.2)
IFG	140 (24.8)
White blood cell count $\times 10^9$ mean (SD)	5.7 (1.6)
Albumin g/dl mean (SD)	4.4 (0.3)
Uric acid mg/dl mean (SD)	4.7 (1.3)
SF-36 Physical score	51.5 (8.0)
SF-36 Mental score	53.1 (7.7)
Sleep, hours per day, n (%)	
<6	45 (8.0)
6–8	490 (87.0)
>8	28 (5.0)
Family history of hypertension, n (%) yes	183 (33.7)
Reported weight change since age 25 (lbs), mean (SD)	26.8(25.9)

Table 2

Selected characteristics according to pre-hypertensive status

	Normotensive	Pre-hypertensive	p-value
	N=375	N=189	
Baseline characteristics			
Age (years), mean (SD)	50.4 (9.9)	54.5 (11.4)	<0.001
Gender, n (%) Female	272 (72.5)	126 (66.7)	0.149
Race/Ethnicity, n (%) Caucasian	361 (96.3)	183 (96.8)	0.735
Smoking status, n (%)			0.919
Never	195 (52.1)	102 (54.0)	
Former	130 (34.8)	63 (33.3)	
Current	49 (13.1)	24 (12.7)	
Drinking status, n (%)			0.427
Abstainer	31 (8.3)	18 (9.6)	
Non-current (not in past 30 days)	72 (19.4)	44 (23.4)	
Current	269 (72.3)	126 (67.0)	
Waist circumference (cm), mean (SD)	83.4 (12.2)	87.2 (13.0)	0.001
Body mass index (kg/m^2), mean (SD)	25.6 (4.1)	27.4 (5.6)	<0.001
MET-hrs in leisure-time activity in past 7 days, mean (SD)	27.0 (27.3)	30.0 (33.0)	0.283
SBP mmHg mean (SD)	105.6 (7.8)	109.2 (6.8)	<0.001
DBP mmHg mean (SD)	66.1 (6.6)	68.2 (6.5)	<0.001
Glycemic Status, n (%):			<0.001
NGT	301 (80.3)	123 (65.1)	
IFG	74 (19.7)	66 (34.9)	
White blood cell count $\times 10^9$ mean (SD)	5.7 (1.5)	5.7 (1.6)	0.841
Albumin g/dl mean (SD)	4.4 (0.3)	4.3 (0.3)	0.086
Uric acid mg/dl mean (SD)	4.5 (1.3)	4.9 (1.4)	0.006
SF-36 Physical score	51.6 (8.2)	51.2 (7.8)	0.754
SF-36 Mental score	52.7 (7.5)	53.9 (8.0)	0.319
Sleep, hours per day, n (%)			0.648
<6	32 (8.6)	13 (6.9)	
6–8	322 (86.1)	168 (88.9)	
>8	20 (5.3)	8 (4.2)	
Family history of hypertension, n (%)yes	126 (34.9)	57 (31.3)	0.404
Reported weight change since age 25 (lbs), mean (SD)	24.8 (22.1)	31.7 (36.9)	0.005

Table 3

Results of Multivariate Stepwise Logistic Regression on Prehypertension

Risk Factors	OR	95% C.I.
IFG (yes, no)	1.70	1.08, 2.69
Weight gain since age 25 (per 10 lbs)	1.12	1.04, 1.21
Age (per year)	1.03	1.01, 1.05
Systolic BP (per 1 mmHg)	1.07	1.03, 1.10