

PULSE PRESSURE—II. FACTORS ASSOCIATED WITH FOLLOW-UP VALUES IN THREE CHICAGO EPIDEMIOLOGIC STUDIES

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Abstract—This report, the second in a series on pulse pressure and pure systolic hypertension, examined in prospective analyses the associations between both the initial values of five variables and the changes in these variables and pulse pressure, utilizing data from three Chicago epidemiologic studies, in order to determine whether variables known to be related to blood pressure and hypertension are related to pure systolic hypertension or 'classical' hypertension. In these analyses, follow-up pulse pressure, which was measured from 2–5 years after the initial measurement of the other variables, was redefined so that the association between the initial value or change and pulse pressure indicated whether the initial value or change was more strongly related to follow-up systolic or diastolic blood pressure. In these three studies, only the initial value for cigarette use had a consistent positive association with follow-up pulse pressure. Change in heart rate was generally positively related to follow-up pulse pressure, while the initial value was not. For relative weight and serum cholesterol, both the change and the initial value tended to be negatively related. For glucose, the association was not consistent for either the initial value or the change. The results from these prospective analyses thus suggest that cigarette use is related to pure systolic hypertension, rather than 'classical' hypertension.

INTRODUCTION

BECAUSE systolic blood pressure rises more sharply with age than diastolic blood pressure for those middle-aged and beyond, leading to an increasing prevalence with advancing age of elevated systolic pressure without elevated diastolic pressure, i.e. so-called pure systolic hypertension, two questions arise in regard to this finding: (1) Are factors which have been shown to be related to the level of blood pressure and hypertension related to pure systolic hypertension and a widened pulse pressure, or to 'classical' hypertension, i.e. to hypertension defined solely on the basis of the level of the diastolic pressure? (2) Do a widened pulse pressure and pure systolic hypertension have prognostic significance over and above that conferred by the level of the diastolic pressure, i.e. is pure systolic hypertension an independent risk factor for the atherosclerotic diseases?

This is the second of a series of reports dealing with these questions utilizing data from four epidemiologic studies in Chicago. The first report in this series examined the associations between several variables and adjusted pulse pressure in cross-sectional analyses, in an effort to determine which variables are more strongly related to systolic, and which to diastolic pressure [1]. The present report, utilizing data from three of the four epidemiologic studies, examines the associations between the initial values of several variables and follow-up adjusted pulse pressure and the associations between the changes in these variables and follow-up pulse pressure, with a time between examinations of 2–5 years.

The variables considered in this report are serum cholesterol, relative weight, heart rate, glucose and cigarette use. These associations are examined among white males and females age 25–64 from the Chicago Heart Association Detection Project in Industry,

and among white males age 27-64 from the Chicago Peoples Gas Company study and age 40-55 from the Chicago Western Electric Company study.

MATERIAL AND METHODS

The epidemiologic studies providing data for this series were described in the first paper [1], and only information pertinent to the analyses presented here is given.

Chicago Heart Association Detection Project in Industry

From the fall of 1967 until early 1973, the Chicago Heart Association Detection Project in Industry screened 39,665 young adult and middle-aged men and women, both white and black, employed by 85 firms in the greater Chicago area. Rescreening was done at 21 companies at which 8800 persons had been screened initially from 8 to 65 months previously. Overall, 47.9% of these 8800 persons, or 4377 men and women, participated in the rescreening project. Of this group 1804 men and women were neither hypertensives nor diabetics on drug treatment for this condition at the initial examination, were not on drug treatment for hypertension at the rescreening examination, had complete baseline data on all relevant variables, and had at least a 24 month time interval between examinations. The analyses of the association between the initial values of the variables and follow-up pulse pressure are restricted to the 1641 white males and females age 25-64 from this group. In the analyses of the associations between changes in the variables and follow-up pulse pressure, 43 men and women were excluded for missing follow-up data, leaving 1598 men and women available for these analyses. Only white males and females age 25-64 are considered here because these are the only age-sex-color groups with numbers sufficient for analysis. Uric acid is not one of the variables examined in this report, because most of the rescreenees were screened initially during the period in which uric acid was not measured.

The data are analyzed for the age groups 25-44 and 45-64.

Chicago Peoples Gas Company study

In the Chicago Peoples Gas Company study, the Gas Company Medical Department examined men age 40-59 in 1958 or 1959, and men age 25-39 over the years 1959-63 with repeat examinations scheduled yearly for men 50-59, every two years for men 40-49, and every four years for men 25-39. Because the younger men were only examined every four years, four years was selected as the time interval between the follow-up blood pressure measurement and the initial measurement of the other variables in this study. In addition, because a thorough effort was made to re-examine all men during the years 1965-67, the examination given during this period was defined as the follow-up examination, and the examination given during the period 1961-63 was defined as the baseline examination.

Of the initial group of 2872 men examined in the two cohorts, 2367 were white males age 27-64 with an examination during the period 1961-63. Of these 2367 men, 1840 had a blood pressure measurement from 36 to 60 months after the examination in 1961-63. If the time interval between measurements was less than 36 months or more than 60 months, the individual was excluded. Of this group of 1840 men, 1412 had complete data on heart rate, serum cholesterol, and weight at the 1961-63 examination. These men are the subjects of the analyses of the association between follow-up pulse pressure and the initial values of the variables for this study. Fifty-five men in this group did not have follow-up data on these variables at the 1965-67 examination and have been excluded in the analyses of the association between follow-up pulse pressure and changes in the variables. Because glucose and uric acid were not measured at the examination given from 1961-63, these variables are not considered in the analyses.

The data are analyzed for the age groups 27-44 and 45-64.

Chicago Western Electric Company study

In the Chicago Western Electric Company study, the men were examined annually. To

provide comparability with the Gas Company, four years was selected as the time interval between examinations for the men in this study also. Of 2107 men age 40-55 originally examined in 1957-58, 1899 had complete baseline data on all relevant variables. Of this group of 1899 men, the 1767 who had a blood pressure measurement at the annual examination four years later are the subjects of the analyses of the association between follow-up pulse pressure and the initial values of the variables. Of this group of 1767, 567 had missing follow-up data on the other variables, and have been excluded in the analyses of the association between follow-up pulse pressure and changes in the variables. Because glucose was not measured at the baseline examination for these men, this variable is not considered in the analyses.

The data are analyzed for the age groups 40-44 and 45-55.

Statistical methods

In the present report, for each age-sex group in each study, the follow-up value for systolic blood pressure was rescaled for each individual in the group by multiplying the individual's follow-up systolic pressure by the ratio of the standard deviations of follow-up diastolic and systolic pressure in the group. An adjusted follow-up pulse pressure was then computed for each individual by subtracting the follow-up diastolic pressure from the rescaled follow-up systolic pressure.

In the first report in this series [1], it was shown that the correlation between a variable and adjusted pulse pressure could be used to determine whether the variable was more strongly related to systolic or diastolic blood pressure. Thus, in the analyses of the association between follow-up pulse pressure and the initial values of the variables, the association between a variable and follow-up adjusted pulse pressure is used to determine whether the variable is more strongly related to follow-up systolic or follow-up diastolic blood pressure. In these analyses, follow-up adjusted pulse pressure is regressed on the initial value of each variable in a separate univariate analysis and then on all variables combined in a multivariate analysis. As in the previous report, the standardized regression coefficients are marked with one, two, or three asterisks depending on whether the absolute value is 0.0500-0.0749, 0.0750-0.0999, or ≥ 0.1000 . Thus, in these analyses, if the coefficient is greater than 0.05, the variable is considered to be more strongly related to follow-up systolic pressure, equally associated with follow-up systolic and diastolic pressure if the value is between -0.05 and +0.05, and more strongly associated with follow-up diastolic pressure if the value is less than -0.05.

In the analyses of the association between follow-up pulse pressure and changes in the variables, the follow-up value of each of the variables under consideration was rescaled by the ratio of the standard deviations of the initial value of the variable and the follow-up value of the variable in each age-sex group. For each individual, the change in a variable was then defined as the difference between the rescaled follow-up value and the initial value. This was done so that the correlation between the change in a variable and follow-up pulse pressure, is a function of the difference between the correlations of the follow-up value of the variable and follow-up pulse pressure, and the initial value of the variable and follow-up pulse pressure. In these analyses, follow-up adjusted pulse pressure is regressed on the change in each variable separately in a univariate analysis and then on the changes in all variables combined in a multivariate analysis. The standardized regression coefficients are marked with one, two, or three asterisks using the same criteria as that described above.

RESULTS

Serum cholesterol. Table 1 presents the regression coefficients from the analyses of the associations between baseline serum cholesterol and follow-up pulse pressure and between the change in serum cholesterol and follow-up pulse pressure for the men and women from the Chicago Heart Association study and the men from the Gas Company and Western Electric studies. The variables included in the multivariate analyses for the initial value in addition to serum cholesterol are age, relative weight, heart or pulse rate

TABLE 1. STANDARDIZED PARTIAL REGRESSION COEFFICIENTS FOR INITIAL SERUM CHOLESTEROL AND FOLLOW-UP PULSE PRESSURE AND CHANGE IN SERUM CHOLESTEROL AND FOLLOW-UP PULSE PRESSURE BY STUDY, AGE AND SEX

Study	Age group	N	Initial value		N	Change	
			Univ	Mult		Univ	Mult
<u>White males:</u>							
Chicago	25-44	747	0.0698*	0.0896**	732	0.0288	0.0201
Heart	45-64	450	-0.0115	-0.0104	435	0.0087	0.0003
Peoples	27-44	560	-0.0086	0.0113	541	-0.0553*	-0.0490
Gas	45-64	852	-0.0770**	-0.0633*	816	-0.0678*	-0.0609*
Western	40-44	506	0.0306	0.0343	331	-0.0087	0.0021
Electric	45-55	1261	-0.0480	-0.0576*	869	0.0272	0.0363
<u>White females:</u>							
Chicago	25-44	195	-0.0805**	-0.0734*	189	-0.0565*	-0.0735*
Heart	45-64	249	0.0348	0.0014	242	-0.0200	-0.0126

*0.0500-0.0749; **0.0750-0.0999; *** ≥ 0.1000 .

and cigarettes/day for each of the three studies, and in addition, plasma glucose 1 hr after a 50 g oral load for the Chicago Heart Association study. The variables included in the multivariate analyses of change, in addition to change in serum cholesterol, are change in heart rate or pulse rate and change in relative weight for each of the three studies, and in addition, change in cigarette use in the Western Electric study, and change in cigarette use and change in glucose in the Chicago Heart Association study.

Baseline serum cholesterol has a significant negative association with follow-up pulse pressure in three of the groups in the multivariate analyses, and a significant positive association in one of the groups. For the other four groups, the coefficients are quite small in both the univariate and multivariate analyses.

Change in serum cholesterol has a significant negative association with follow-up pulse pressure in three of the groups in the univariate analyses, and in two in the multivariate.

Relative weight. The regression coefficients for relative weight and change in relative weight are given in Table 2. The association between initial relative weight and follow-up pulse pressure is negative in 7 of the 8 groups, including all 6 groups of males, with the coefficient being significantly negative in three groups in the multivariate analyses. However, for the white females age 45-64 from the Chicago Heart Association study, the association is significantly positive, indicating that baseline relative weight is more strongly associated with follow-up systolic pressure in these women.

TABLE 2. STANDARDIZED PARTIAL REGRESSION COEFFICIENTS FOR INITIAL RELATIVE WEIGHT AND FOLLOW-UP PULSE PRESSURE AND CHANGE IN RELATIVE WEIGHT AND FOLLOW-UP PULSE PRESSURE BY STUDY, AGE AND SEX

Study	Age group	N	Initial value		N	Change	
			Univ	Mult		Univ	Mult
<u>White males:</u>							
Chicago	25-44	747	-0.0044	-0.0084	732	0.0228	0.0179
Heart	45-64	450	-0.0209	-0.0182	435	-0.0142	-0.0182
Peoples	27-44	560	-0.1092***	-0.0967**	541	-0.0574*	-0.0532*
Gas	45-64	852	-0.1109***	-0.0973**	816	-0.0607*	-0.0514*
Western	40-44	506	-0.0662*	-0.0716*	331	-0.1063***	-0.1178***
Electric	45-55	1261	-0.0513*	-0.0378	869	-0.0614*	-0.0669*
<u>White females:</u>							
Chicago	25-44	195	-0.0257	-0.0031	189	0.1727***	0.1768***
Heart	45-64	249	0.1100***	0.0869**	242	-0.0458	-0.0484

*0.0500-0.0749; **0.0750-0.0999; ***0.1000.

TABLE 3. STANDARDIZED PARTIAL REGRESSION COEFFICIENTS FOR INITIAL HEART RATE AND FOLLOW-UP PULSE PRESSURE AND CHANGE IN HEART RATE AND FOLLOW-UP PULSE PRESSURE BY STUDY, AGE AND SEX

Study	Age group	N	Initial value		N	Change	
			Univ	Mult		Univ	Mult
<u>White males:</u>							
Chicago	25-44	747	0.0434	0.0198	732	0.1420***	0.1472***
Heart	45-64	490	-0.0254	-0.0380	435	0.0928***	0.0929***
Peoples	27-44	560	0.0262	0.0285	541	0.0140	0.0256
Gas	45-64	852	0.0043	-0.0060	816	-0.0229	-0.0110
Western	40-44	506	-0.0003	-0.0090	331	0.0910**	0.1039***
Electric	45-55	1261	-0.0325	-0.0385	869	0.0047	0.0058
<u>White females:</u>							
Chicago	25-44	195	0.0362	0.0508*	189	0.1398***	0.1429***
Heart	45-64	249	0.1229***	0.1442***	242	0.1078***	0.1194***

*0.0500-0.0749; **0.0750-0.0999; *** \geq 0.1000.

Change in relative weight is negatively related to follow-up pulse pressure in 6 of the 8 groups, and positively related in the other two, with both groups being under the age of 45. The coefficients exceed the levels established for significance, however, in only four of the 6 groups in which the coefficient is negative, and in one of the two groups in which the coefficient is positive.

Heart rate. The coefficients corresponding to heart rate are presented in Table 3. Among white males, initial heart rate is not significantly related to follow-up pulse pressure in any of the groups. In these 6 groups, heart rate appears to be equally related to follow-up systolic and diastolic pressure. However, among white females, heart rate has a significant positive association with follow-up pulse pressure in the multivariate analyses in both groups.

Change in heart rate has a significant positive association with follow-up pulse pressure in 5 of the 8 groups, indicating that follow-up heart rate is more strongly related to follow-up pulse pressure than baseline heart rate.

Glucose. The regression coefficients for glucose for the men and women from the Chicago Heart Association study are presented in Table 4. Among men and women 45-64 glucose has a positive association with follow-up pulse pressure. However, for women 25-44 glucose has a significant negative association with follow-up pulse pressure.

Change in glucose has a significant positive association with follow-up pulse pressure in the two groups of women. In the men, change in glucose is not related to follow-up pulse pressure.

TABLE 4. STANDARDIZED PARTIAL REGRESSION COEFFICIENTS FOR INITIAL GLUCOSE AND FOLLOW-UP PULSE PRESSURE AND CHANGE IN GLUCOSE AND FOLLOW-UP PULSE PRESSURE BY STUDY, AGE AND SEX

Study	Age group	N	Initial value		N	Change	
			Univ	Mult		Univ	Mult
White males:							
Chicago Heart	25-44	747	0.0057	0.0068	732	-0.0287	-0.0363
	45-64	450	0.0408	0.0499	435	0.0005	-0.0118
White females:							
Chicago Heart	25-44	195	-0.1581***	-0.1614***	189	0.2425***	0.2329***
	45-64	249	0.0208	-0.0581*	242	0.0986**	0.1077***

*0.0500-0.0749; **0.0750-0.0999; *** \geq 0.1000.

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TABLE 5. STANDARDIZED PARTIAL REGRESSION COEFFICIENTS FOR INITIAL CIGARETTE USE AND FOLLOW-UP PULSE PRESSURE AND CHANGE IN CIGARETTE USE AND FOLLOW-UP PULSE PRESSURE BY STUDY, AGE AND SEX

Study	Age group	N	Initial value		N	Change	
			Univ	Mult		Univ	Mult
<u>White males:</u>							
Chicago	25-44	747	0.0891**	0.0816**	732	-0.0023	0.0012
Heart	45-64	450	0.0328	0.0419	435	0.0374	0.0359
Peoples	27-44	560	0.1020***	0.0911**	—	—	—
Gas	45-64	852	0.0588*	0.0776**	—	—	—
Western	40-44	506	0.0959**	0.0959**	331	-0.0101	-0.0182
Electric	45-55	1261	0.0784**	0.0908**	869	-0.0001	-0.0063
<u>White females:</u>							
Chicago	25-44	195	-0.0034	0.0057	189	0.0127	0.0019
Heart	45-64	249	0.0083	0.0458	242	-0.0765**	-0.0879**

*0.0500-0.0749; **0.0750-0.0999; *** ≥ 0.1000 .

Cigarettes/day. Table 5 gives the regression coefficients for cigarettes/day. Since data on cigarette use are not available on the Gas Company men from the 1965-67 examination, the association between change in number of cigarettes smoked and follow-up pulse pressure could not be computed for these men. As in the previous report [1], the coefficients for cigarettes/day in the multivariate analysis are from a model that did not include heart rate. Among white males the coefficients for initial cigarette use are positive in all 6 age groups, and greater than 0.05 in 5 of the groups. For the white females, although the coefficients for both groups are positive in the multivariate analyses, neither is larger than 0.05.

In general, change in cigarette use is not related to follow-up pulse pressure. However, there is a negative association among white females age 45-64.

DISCUSSION

This is the second of a series of papers dealing with pulse pressure and pure systolic hypertension. The first paper in this series examined the associations between several variables and pulse pressure in cross-sectional analyses [1], with pulse pressure redefined so that the association between a variable and pulse pressure indicated whether the variable was more strongly related to systolic or diastolic blood pressure. The purpose of these analyses was to determine whether variables which have been shown to be related to the level of blood pressure and hypertension, are in fact related to a widened pulse pressure and pure systolic hypertension, or to 'classical' hypertension, i.e. hypertension defined solely on the basis of the level of the diastolic pressure. Each of the variables considered in the prospective analyses of the present report was also considered in the first report, and has been shown to be a correlate of blood pressure and/or a risk factor for the development of hypertension [2-21].

In the cross-sectional analyses from these studies, glucose, heart rate, and cigarette use tended to show a stronger association with systolic than diastolic blood pressure, suggesting a possible role for these variables in pure systolic hypertension, while serum cholesterol tended to be more strongly related to the diastolic pressure, suggesting an association with 'classical' hypertension. In addition, relative weight tended to be more strongly associated with systolic pressure in men and women under the age of 35, and more strongly associated with diastolic pressure in men and women age 45 and over.

The goal of the present report was to determine whether or not the associations observed in cross-sectional analyses between these variables and pulse pressure are also present prospectively, i.e. are the changes in these variables more strongly related to systolic or diastolic blood pressure? And are these variables more strongly related to

subsequent systolic or diastolic blood pressure, when measurement of the variables precedes the measurement of the blood pressure by two to five years?

In this regard the initial value for cigarettes/day was generally more strongly related to follow-up systolic than follow-up diastolic pressure, while the change in cigarette consumption was generally equally related to follow-up systolic and diastolic pressure. The initial value for heart rate was not related to follow-up pulse pressure in the men, indicating an equal association with follow-up systolic and diastolic blood pressure, although there was a positive association in both groups of women. Change in heart rate was generally positively related to follow-up pulse pressure. Both change in serum cholesterol and the initial value for serum cholesterol tended to be related equally to follow-up systolic and diastolic pressure, or more strongly related to diastolic pressure. Both change in relative weight and the initial value for relative weight were negatively related to follow-up pulse pressure, although both variables showed a significant positive association in one group of women. Change in glucose had a significant positive association with follow-up pulse pressure in the two groups of women, and the initial value for glucose had a significant negative association in these two groups. Among the men, both the change and initial value were equally related to follow-up systolic and diastolic pressure.

Thus, the results of the prospective analyses considered here generally confirm the findings in the cross-sectional analyses in regard to the variables, serum cholesterol and relative weight, i.e. these two variables appear to be more strongly related to diastolic rather than systolic blood pressure, and thus to 'classical' hypertension rather than pure systolic hypertension. For the other three variables, the results of the prospective analyses are not entirely consistent with the results of the cross-sectional analyses. For heart rate, while changes in heart rate generally showed a positive association with follow-up pulse pressure, prior values generally showed no association, suggesting that only the current value of heart rate is more strongly related to systolic blood pressure. Thus, high heart rate may be a concomitant of a widened pulse pressure and pure systolic hypertension, rather than a precursor.

Since the initial value for glucose did not show a significant positive association with follow-up pulse pressure in any of the four groups, it would also appear that only the current value of glucose is associated with a widened pulse pressure. Such a conclusion must be made with caution, however, since the sample sizes in the prospective analyses are much smaller than those in the cross-sectional analyses, and since the positive associations between glucose and adjusted pulse pressure observed in the cross-sectional analyses were primarily in the Gas Company, Western Electric, and Chicago Health Department studies, rather than the Chicago Heart Association study, which provided the data for the prospective analyses.

The results for cigarettes/day do, however, confirm the findings of the cross-sectional analyses, since prior consumption tends to be more strongly related to follow-up systolic than follow-up diastolic pressure. The fact that change in cigarette consumption is not related to pulse pressure in these studies indicates that prior cigarette use is as strongly related to a widened pulse pressure as is current consumption.

Thus, since cigarette use is related more strongly to systolic than diastolic blood pressure in both cross-sectional and prospective analyses, it seems likely that cigarette use is related to a widened pulse pressure and pure systolic hypertension, rather than 'classical' hypertension. An association between cigarettes and a widened pulse pressure may reflect an increased peripheral resistance among smokers, or the presence of aortic atherosclerosis and arterial inelasticity, since smoking is a risk factor for the atherosclerotic diseases [22].

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