Do Depression Symptoms Predict Early Hypertension Incidence in Young Adults in the CARDIA Study?

Karina Davidson, PhD; Bruce S. Jonas, PhD; Kim E. Dixon, RN, MBA; Jerome H. Markovitz, MD, MPH

Background: Hypertension has been linked to several psychological factors, including depression, but the relation between hypertension incidence and depressive symptoms has not been adequately examined.

Objective: To determine if depressive symptoms independently predict hypertension incidence.

Design and Setting: A prospective, multicenter, epidemiological cohort of young adults (aged 23-35 years at study entry) from the general community without hypertension followed up for 5 years.

Subjects: A sample of 3343 adults from 4 urban areas stratified for race (black and white) from the CARDIA (Coronary Artery Risk Development in Young Adults) study.

Main Outcome Measure: Hypertension incidence, which was defined as blood pressure higher than 160/95 mm Hg (assessed on a single occasion) or the use of prescribed antihypertensive medication.

Results: Participants with high scores ($\geq 16$) on the Center for Epidemiological Studies Depression (CES-D) Scale were at significant risk for hypertension incidence compared with those with low CES-D scores ($\leq 7$; odds ratio, 2.10; 95% confidence interval, 1.22-3.61) after adjustment for other hypertension risk factors (eg, age, resting systolic blood pressure at the 5-year examination, physical activity, daily alcohol use, parental history of hypertension, education, presence of diabetes mellitus or heart disease, sex, and race) in fixed logistic models. Those with intermediate depressive symptoms (CES-D scores 8-15) were also at significant risk (adjusted odds ratio, 1.78; 95% confidence interval, 1.06-2.98). These associations were significant in blacks alone but were not found in whites, who had a lower hypertension incidence (29 [2%] of 1806) than blacks (89 [6%] of 1537).

Conclusions: Depressive symptoms were predictive of later hypertension incidence in young adults, and young blacks with depressive symptoms were at high risk of developing hypertension.

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Hypertension is one of the most prevalent diseases among young generally healthy adults in the United States. However, hypertension prevalence is not uniformly distributed across the population; blacks are at increased risk for hypertension, with incidence and prevalence studies suggesting a risk approximately 2 to 3 times higher than that in whites. Black women aged 25 to 34 years have the highest hypertension incidence rates; black men and women have double the hypertension prevalence rate of their white counterparts by the age of 25 years. Known risk factors for hypertension, such as physical inactivity, parental history of hypertension, or age, do not explain this increased risk.

Depression has been proposed as a likely risk factor for hypertension and coronary heart disease (CHD). Depression has recently been found to predict recurrence of and mortality due to myocardial infarction in a series of studies and hypertension incidence in a prospective population-based study. The relation between depression and hypertension is biologically plausible given the increased adrenergic activity in depression that may have a pressor effect on the cardiovascular system. However, several cross-sectional and prospective studies reported no relation between depression and hypertension.

For example, in a cross-sectional analysis of the 5-year data from the CARDIA (Coronary Artery Risk Development in Young Adults) study, depression...
SUBJECTS AND METHODS

The CARDIA study\textsuperscript{17} was a longitudinal, multicenter epidemiological investigation designed to determine the precursors of the risk factors of CHD in young adults. The subjects of the CARDIA study were initially recruited in 1985 and 1986. A total of 5115 young adults aged 18 to 30 years were recruited in 4 cities. The subjects were divided into groups that were approximately balanced for age (18-24 and 25-30 years), sex, race (black and white), and educational level (high school graduate or less and beyond high school). The study design and baseline characteristics of the subjects have been previously described in detail.\textsuperscript{17,18} Baseline psychological testing was administered at the 5-year examination (1990-1991), when subjects were aged 23-33 years, and we examined levels of hypertension incidence 5 years later at the 10-year examination.

Of the 5115 originally enrolled in the first year, 3730 participated in both the 5- and 10-year examinations. At the 5-year examination, subjects were excluded for the following reasons: pregnancy (n=28), missing hypertension risk factor data (n=213), treatment of hypertension (n=37), and presence of hypertension (n=53; defined as systolic BP >160 mm Hg or diastolic BP >95 mm Hg). At the 10-year examination, 28 subjects were excluded because of pregnancy. As some persons met multiple exclusion criteria, 385 subjects were excluded. The overall remaining sample size was 3343 (904 black women, 633 black men, 936 white women, and 870 white men).

MEASURES

Depressive symptoms were obtained at the baseline or 5-year examination, as assessed by the CES-D Scale, a well-standardized instrument that has been used extensively in other studies.\textsuperscript{19-21} Sample items included “I felt sad” or “I had crying spells,” and subjects indicated the frequency for each item for the past week. The high depressive symptom group included subjects with a CES-D score of 16 or higher, and the low depressive symptom group included subjects with a CES-D score of 7 or less. The intermediate depressive symptom group included subjects whose scores were between those 2 CES-D cutoff scores.

A number of standard hypertension risk factors were also assessed at the 5-year examination. Using a questionnaire, the following information was obtained: age; years of education; smoking status (current smokers vs ex-smokers and nonsmokers); alcohol consumption (milliliters per day); parental history of hypertension (present vs absent); and medical history of diabetes mellitus, heart problems, or prior myocardial infarction (presence of any vs absence of all). Physical inactivity was determined using a standard questionnaire in which approximate energy expenditure for all activities was calculated in exercise units and consisted of a sum of moderate and vigorous intensity scores.\textsuperscript{22-24} Less than 200 exercise units per week was defined as physically inactive using this measurement.\textsuperscript{21} Exercise units in turn were correlated with treadmill endurance and skinfold thickness in this sample.\textsuperscript{24} Body mass index was obtained with subjects dressed in lightweight clothing without shoes. These hypertension risk factors were included in the logistic models predicting hypertension incidence, as all previously were found to be associated with the development of hypertension and constituted a suitable list of potential confounders.\textsuperscript{23}

Blood pressure was assessed in the morning for the 5-year and follow-up examinations. After a 5-minute rest, BP was assessed at three 1-minute intervals on the right arm of the seated subjects with a random zero sphygmomanometer.\textsuperscript{14,17,18} First- and fifth-phase Korotkoff sounds were recorded, and the mean of the second and third BP measurements obtained at the same session was used in the following analyses. Hypertension incidence was defined according to the following criteria, which were used in previous studies\textsuperscript{24-26}: a mean systolic BP higher than 160 mm Hg; a mean diastolic BP higher than 95 mm Hg; or the use of antihypertensive medication at the 5-year follow-up.

STATISTICAL ANALYSES

Statistical software (SAS version 6.12; SAS Institute Inc, Cary, NC) was used to analyze the data. Percentage agreement was calculated to check the stability of the depressive symptom group status from the 5-year examination to 5 years later. t Tests and $\chi^2$ tests were used to test for race differences in continuous and dichotomous 5-year hypertension risk factors, respectively. $\chi^2$ Tests were also used to test for depressive symptom group differences in hypertension incidence. Age-adjusted odds ratios (ORs) for depressive group status were calculated through a fixed logistic model (PROC LOGISTIC version 3; SAS Institute Inc) in which depressive groups were entered as 2 dummy variables, with high and intermediate depressive symptom groups contrasted with the low depressive symptom group. Odds ratios were then recalculated for the depressive symptom groups adjusting for all 5-year hypertension risk factors. Odds ratios for all continuous variables (age, body mass index, and 5-year systolic BP) were calculated based on a movement of 1 SD. Physical activity, smoking status, parental history of hypertension, presence of diabetes mellitus or heart disease, sex, and race were all dummy coded so that the hypothesized exposure category was 1 and the hypothesized low-risk category was 0.
subjects aged 45 to 64 years (relative risk, 1.82) and for black subjects aged 25 to 64 years (relative risk, 2.99).

The CARDIA prospective cohort study was designed, in part, to allow examination of risk factor development in young healthy black and white adults. Thus, it remedied a number of problems noted in previously reported studies: it was prospective; it included young black and white men and women; and, at the 5-year follow-up examination, the depressive symptom level was assessed. In the present study, we determined if the level of depressive symptoms was independently predictive of hypertension onset in a young healthy sample and in separate race groups.

**RESULTS**

**FIVE-YEAR HYPERTENSION RISK FACTORS**

The risk factor levels or percentages at the 5-year examination are shown for the full sample and the black and white cohorts in Table 1. The risk factors in the black cohort were significantly higher than those of the white cohort except for alcohol use and diabetes mellitus or heart disease. The percentage of subjects (53%) with a parental history of hypertension may seem high, but it is similar to that (56%) derived from the 1998 data set available from the National Center for Health Statistics.30 As we did not find any interactions between depressive symptom group and sex in any model, we did not show the risk factors separately for men and women.

**HYPERTENSION INCIDENCE AND DEPRESSIVE SYMPTOM GROUPS**

The hypertension incidence by depressive symptom group is shown in Table 2. Hypertension incidence was significantly more elevated in the high and intermediate depressive symptom groups than in the low depressive symptom group for both the full sample and the black cohort. There were far more subjects with hypertension in the black cohort (n = 89) than in the white cohort (n = 29). Of the subjects classified as having hypertension, 47% used antihypertensive medication, 51% had a resting diastolic BP higher than 95 mm Hg, and 1% had a resting systolic BP higher than 160 mm Hg. Finally, 1% of the subjects met both the diastolic and systolic BP criteria. The percentages of black and white subjects who met the hypertension incidence criteria were similar.

The prevalence of CES-D scores of 16 or higher at the 5-year examination was high: 29% of the black cohort and 18% of the white cohort reported symptoms in this range.19 Subsyndromal depressive levels (CES-D scores 8-15) were similarly prevalent in the black cohort (38%) and the white cohort (36%). Depressive symptom group stability from the 5- to 10-year examination was moderate, with 54% remaining in the same depressive symptom group more than 5 years, and an additional 40% of the sample moving into the contiguous depressive symptom group (low to intermediate and intermediate to low or high).

**RISK OF HYPERTENSION**

For the entire sample, the age-adjusted ORs were significant for the high depressive group (OR, 2.83; 95% confidence interval [CI], 1.74-4.59) and for the intermediate depressive group (OR, 1.89; 95% CI, 1.18-3.03). Among blacks, the high depressive symptom group had an age-adjusted OR of 2.70 (95% CI, 1.49-4.92), and the intermediate depressive symptom group had an OR of 2.05 (95% CI, 1.14-3.70); the age-adjusted ORs for the white high depressive symptom group (OR, 1.52; 95% CI, 0.52-3.92) and the intermediate depressive symptom group (OR, 1.15; 95% CI, 0.49-2.69; P >.05) were only moderately elevated and were not statistically significant.

Table 3 presents the adjusted ORs for all hypertension risk factors listed in Table 1, as well as for the high and intermediate depressive symptom groups. For the full sample, the ORs for both high and intermediate depressive symptom groups remained significant compared with those in the low depressive symptom group.
Table 3. Odds Ratios (ORs) for Hypertension Incidence*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td>All (N = 3343)</td>
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<tr>
<td>High depressive symptoms</td>
<td>2.10† (1.22-3.61)</td>
</tr>
<tr>
<td>Intermediate depressive symptoms</td>
<td>1.78† (1.06-2.98)</td>
</tr>
<tr>
<td>Age (continuous)</td>
<td>1.77† (1.41-2.20)</td>
</tr>
<tr>
<td>BMI (continuous)</td>
<td>1.35† (1.15-1.57)</td>
</tr>
<tr>
<td>5-y SBP (continuous)</td>
<td>3.00† (2.46-3.68)</td>
</tr>
<tr>
<td>Years of education (continuous)</td>
<td>0.84 (0.66-1.07)</td>
</tr>
<tr>
<td>Alcohol use (continuous)</td>
<td>1.08 (0.94-1.25)</td>
</tr>
<tr>
<td>Physically inactive</td>
<td>1.59† (1.04-2.43)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.75 (0.46-1.22)</td>
</tr>
<tr>
<td>Parental history of hypertension</td>
<td>2.67† (1.65-4.34)</td>
</tr>
<tr>
<td>Diabetes mellitus or heart disease</td>
<td>1.62 (0.90-2.92)</td>
</tr>
<tr>
<td>Male</td>
<td>0.79 (0.50-1.26)</td>
</tr>
<tr>
<td>Black</td>
<td>2.15† (1.33-3.46)</td>
</tr>
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</table>
An alternative definition of hypertension incidence was also analyzed. We considered this a liberal definition of hypertension, given that we had only a single BP measurement session during the follow-up examination. Depressive symptoms predicted hypertension in the age-adjusted analyses for the whole cohort, but intermediate depressive symptoms were more consistently related to hypertension incidence in the risk-adjusted analyses. Thus, from these 2 different definitions of hypertension, we concluded that the effects of depressive symptoms were more consistent and stronger when a more conservative definition of hypertension was used. Failure to show a consistent association between depressive symptoms and hypertension for this alternative definition may be attributable to the limited power of the analysis because of both the loss of total subjects available for the analysis and the small number of subjects who had both high depressive symptoms and hypertension.

Both intermediate and high depressive symptoms were significant in predicting conservatively defined hypertension incidence during the 5-year follow-up, suggesting that both subsyndromal and clinical depressive symptom levels may be implicated in hypertension onset. Dimsdale pointed out that even subsyndromal depression can have important health consequences. Subjects with subsyndromal depressive symptoms observed in this and other studies have a high prevalence of hypertension, suggesting that even modest increases in risk for hypertension in these groups may have substantial public health costs.

Our findings and others linking depression and prospective hypertension are in contrast to the null results reported in many cross-sectional analyses. However, our prospective results are consistent with a number of recent findings that depression is independently associated with increased CHD incidence. Thus, there is converging evidence that depression is an independent predictor of cardiovascular morbidity. Many of the studies of CHD and depression do not adjust for hypertension status or BP changes when modeling CHD incidence. Future studies should do so because hypertension may be one of the mechanisms through which depression affects CHD.

The association between depression and hypertension is biologically plausible. For example, there is substantial evidence that the regulation of adrenergic activity often fails in those with clinical depression and such adrenergic alterations may play a role in sustaining BP elevations over time. However, these mechanisms have not been definitively demonstrated, and future research must explore these pathways. In addition, depression may have an impact on behavior, such as adherence to healthy behaviors and general self-care. Others have found that depressive symptoms were significantly associated with unhealthy behaviors in this sample at the 5-year examination. However, we found that depressive symptoms predicted hypertension incidence when controlling for some of the known behavioral hypertension risk factors (such as smoking status and body mass index). It is possible that depressive symptoms alter the level of these behaviors over time (eg, the higher the depressive symptoms, the less physically active over time), and depressive symptoms also could be mutually influenced by behavioral hypertension risk factors (ie, decreased physical activity leads to higher depressive symptoms, and then higher depressive symptoms lead to further decreases in physical activity). However, obtaining data at only 2 examinations does not allow a test of the latter mutual influence hypothesis. It is also possible that there are genetic associations between the tendency to develop depression as well as hypertension and that although depressive symptoms precede hypertension onset, they do not play a causal role in hypertension development. Finally, depressive symptoms might affect other health behaviors that were not assessed in CARDIA, such as overall diet or high-salt or low-potassium intake. It is likely that there are multiple mechanism pathways underlying the relation between depression and hypertension, and physiological and behavioral mechanisms and alternative explanations should be considered in future studies.

There are 3 possible limitations of this study that must be considered. First, although self-reported depressive symptoms allow the opportunity to assess depression in large epidemiological studies, examination of the prospective relation between an interview-based, professional, clinical diagnosis of depression and hypertension is also needed. Second, given the lower hypertension incidence in the white group, a longer follow-up is clearly needed to assess whether the relation found for young blacks is also present in young whites. It is also possible that this relation was unique to blacks; however, the test of this alternative hypothesis, too, requires more white subjects with hypertension. Third, although the analyses show that symptoms of depression may predict development of early hypertension among young blacks, replication clearly is required to firmly establish depression as a risk factor for hypertension in this group.

Blacks in the United States have the highest rates of morbidity and mortality due to cardiovascular disease in the world, and much of this excess risk is due to the increased risk of hypertension in blacks. Predictors of hypertension in this group have been understudied and of the tendency to focus on whites in past epidemiological studies, we have few data with which to explore the possible causes. Depressive symptoms may be an important marker for future hypertension in young blacks; therefore, evaluation of depression in this group may be especially important in assessing risk for hypertension and, by extension, cardiovascular disease.

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Reprints: Karina Davidson, PhD, The Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai Medical Center, One Gustave L. Levy Place, Box 1030, New York, NY 10029-6574 (e-mail: kdavids@bama.u.edu).