Hypertension Among Siblings of Persons With Premature Coronary Heart Disease

Lisa R. Yanek, Taryn F. Moy, Roger S. Blumenthal, Judith V. Raqueño, Raphael M. Yook, Martha N. Hill, Lewis C. Becker, Diane M. Becker

Abstract—To determine the extent to which the Fifth Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC-V) guidelines were implemented in high-risk families with premature coronary heart disease, we examined the prevalence of hypertension and associated coronary risk factors in asymptomatic siblings of persons with documented premature coronary disease (<60 years of age). A total of 859 apparently healthy siblings (51% male, 19% African American) were screened for coronary risk factors. Siblings were classified as normotensive or hypertensive (BP ≥140/90 and/or current antihypertensive pharmacotherapy). The prevalence of hypertension, awareness, treatment, and control among siblings was compared with published national estimates from the third National Health and Nutrition Examination Survey. The prevalence of hypertension in siblings was 44%. Among all hypertensives, only 60% were aware of being hypertensive, 45% were being treated, and 16% were under control. A high prevalence of other coronary risk factors was found among hypertensive siblings: 72% were hypercholesterolemic; 61% were obese; 29% were current smokers; 82% were consuming ≥30% of calories from fat; and only 14% were participating in vigorous physical activity three or more times per week. Comparisons with the national reference population revealed siblings to have a significantly higher prevalence of hypertension, along with significantly lower levels of awareness, treatment, and control. These findings demonstrate the intersection of multiple risk factors among hypertensive siblings and emphasize the need for more aggressive screening and treatment in this easily identifiable high-risk population. (Hypertension. 1998;32:123-128.)

Key Words: blood pressure ■ prevalence ■ hypertension, detection and control ■ risk factors ■ family

The newly released Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure again emphasizes the importance of increased BP levels as a risk factor for cardiovascular disease.1-4 Some populations have shown clear benefit of the JNC guidelines and the efforts of the NHBPEP for detection and treatment of hypertension. It is not clear to what extent this has been true in families at very high risk for CHD, particularly at a young age.

First-degree relatives of persons with premature CHD have been shown to have a 2-fold to 12-fold increased risk of CHD.5-8 Among primary relatives, siblings of persons with clinically documented CHD bear the highest risk for future CHD events,7 and they have also been shown to have a high prevalence of multiple CHD risk factors.8

High BP is well known to be a major modifiable risk factor for CHD.9 Accordingly, the NHBPEP was established in 1972, and the first JNC report was released in 1977, with the most recent update in 1997 (JNC-VI).10-11 National trends have shown increasing awareness, treatment, and control of hypertension.12-14 We have observed low levels of perceived risk for cardiovascular disease in prior studies of siblings of patients with premature CHD,15 suggesting also that the levels of awareness, treatment, and control of hypertension among siblings might also be low. Furthermore, our prior studies have shown a high prevalence of other known risk factors in siblings (D.M.B., R.M.Y., T.F.M., R.S.B., L.C.B., unpublished data, 1997). Given siblings' high relative risk for premature CHD, we designed this study to examine (1) the prevalence of hypertension according to the JNC-V guidelines, (2) awareness, treatment, and control, and (3) the prevalence of additional risk factors in all apparently healthy siblings of persons with premature CHD.

Methods

Sample

Persons with premature CHD (<60 years of age) were identified during hospitalization for a documented CHD event (acute myocardial infarction, coronary artery bypass surgery, coronary angioplasty, or angina with angiographic documentation of at least 1 coronary artery with ≥50% stenosis) in 1 of 7 Baltimore area hospitals.
Hypertension Among Siblings

Selected Abbreviations and Acronyms

BMI = body mass index
BP = blood pressure
CHD = coronary heart disease
CI = confidence interval
DBP = diastolic blood pressure
JNC = Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure
NHANES = National Health and Nutrition Examination Survey
NHBPEP = National High Blood Pressure Education Program
OR = odds ratio
SBP = systolic blood pressure

Measurement

Written informed consent was received from all siblings, and the approval of the Johns Hopkins Medical Institutions Joint Committee on Clinical Investigation was received for all procedures. Eligible siblings underwent a physical examination, phlebotomy, anthropometric and BP measurements, and a resting ECG.

After participants had fasted for at least 12 hours overnight, venipuncture was performed to obtain blood samples for direct measurements of serum levels of total cholesterol, HDL cholesterol, triglycerides, and glucose. LDL cholesterol levels were calculated using the Friedewald equation for those subjects with triglyceride levels lower than 4.52 mmol/L (400 mg/dL). All lipid measurements were performed in the Johns Hopkins Chemistry Laboratory using Lipid Research Program methods. Quality control was maintained by the Johns Hopkins Lipid Research Clinic Laboratory according to Centers for Disease Control standards. The coefficient of variation for cholesterol measurement is 5%, in this laboratory.

Anthropometric measurements were obtained with subjects in light clothing, without shoes. Height was measured on a stadiometer, and weight on a balance scale. BMI was calculated as weight (kg) divided by height (m) squared.

Demographic information, self-reported medical history, medication use, and smoking information were obtained from a standardized interview. Self-reported smoking status was confirmed by exhaled carbon monoxide levels (>8 ppm indicated a current smoker). Dietary information was obtained in a subsample (n=534) using a modified Block Food Frequency Questionnaire characterizing intake in the previous month. Physical activity was assessed in a subsample (n=428) using questions from the Health Insurance Plan of New York questionnaire.

BP was measured using a standard mercury sphygmomanometer, following the American Heart Association and JNC guidelines. The mean of three resting BP readings, taken early morning, midday, and late afternoon during the screening day was used to characterize BP. Hypertension was defined as the subject having a mean SBP of ≥140 mm Hg, a mean DBP of ≥90 mm Hg, and/or currently taking an antihypertensive medication. This is the standard for defining hypertension for the purpose of examining awareness, treatment, and control.

JNC-V Report

JNC-V, published in 1993, included updated recommendations for classification and management of hypertension. The definition of hypertension (BP ≥140/90 mm Hg) has not changed since the first JNC report in 1977; however, JNC-V described “stages” of hypertension for the first time. Treatment guidelines were refined and encouraged a combination of aggressive lifestyle modifications before pharmacological interventions. JNC-VI continued this stage classification and intervention combination, while placing more emphasis on prevention and the discrimination of risk groups.

Siblings were classified according to JNC-V guidelines: optimal (BP <120/80 mm Hg); normal (SBP 120 to 129 mm Hg, DBP 80 to 84 mm Hg); high normal (SBP 130 to 139 mm Hg, DBP 85 to 89 mm Hg); stage 1 or mild hypertension (SBP 140 to 159 mm Hg, DBP 90 to 99 mm Hg); stage 2 or moderate hypertension (SBP 160 to 179 mm Hg, DBP 100 to 109 mm Hg); stage 3 or severe hypertension (SBP 180 to 209 mm Hg, DBP 110 to 119 mm Hg); and stage 4 or very severe hypertension (SBP ≥210 mm Hg, DBP ≥120 mm Hg). When systolic and diastolic pressures led to different categorizations, individuals were classified into the higher stage. The only difference between JNC-V and JNC-VI in terms of classification of stages is that JNC-VI combines stages 3 and 4 because of the rarity of stage 4 hypertension.

NHANES III

NHANES III was designed to estimate the prevalence of certain diseases and conditions in the civilian, noninstitutionalized population of the United States. This survey collected data through interviews and direct examinations and was conducted during 2 phases. The first phase, which took place from 1988 to 1991, was used as a reference population for comparison of prevalence, awareness, treatment, and control among hypertensives. NHANES III assessment and analysis methods have been described in detail elsewhere.

Analyses

All analyses were performed using the SAS software. Comparisons were made by contingency table arrays and were analyzed using the χ2 statistic for categorical variables and Student’s t test for continuous data. Multiple logistic regression was used to obtain adjusted ORs; 95% CIs were then calculated.

Results

Sample Characteristics

A total of 859 siblings from 490 families (mean, 1.8±1 siblings per family) were included in this analysis. Eligible siblings were enrolled into the Johns Hopkins Sibling Study between 1983 and 1996. The sample was 51% female, 19% African American, with a mean age of 45.8±7 years (range, 30 to 59 years). The average educational level completed was 12.7±3 years, with 78% of the siblings having completed high school. The overall prevalence of CHD risk factors was high, with mean levels of total and LDL cholesterol and triglycerides exceeding national averages and mean levels of HDL cholesterol falling below national averages.

Hypertension

Using the JNC-V definitions, 37% of all siblings (n=479 of 859) were classified as currently hypertensive: 27% were stage 1, 9% were stage 2, and 1% were stage 3 or 4. Only 15% of all siblings had optimal BP, while 22% were normal and 26% were classified as high normal. Including those siblings who were currently taking antihypertensive medications but were under control, 44% of the sample (n=380 of 859) was classified as hypertensive. The overall mean SBP was 133.0±16 mm Hg, and the overall mean DBP was 84.6±10 mm Hg for the total group of 859 siblings.
Males tended to have a higher prevalence of hypertension (crude OR = 1.27, 95% CI = 0.97 to 1.7). African Americans were significantly more likely than whites to be hypertensive (crude OR = 1.67, 95% CI = 1.19 to 2.35). The prevalence of hypertension increased as decade of age increased ($\chi^2$ for trend = 62.9, $P$ = 0.001).

A high prevalence of other CHD risk factors was observed among those found to be hypertensive (Table 1). When adjusting for age, hypertensive siblings were significantly more likely than normotensive siblings (BP $\geq$ 140/90 mm Hg) to be obese (for women, BMI $\geq$ 27.3; for men, BMI $\geq$ 27.8) and to have elevated total cholesterol, triglyceride, and LDL cholesterol levels. There was no difference in the prevalence of high fat diets ($\geq$ 30% of calories from fat) or vigorous physical activity ($\geq$ 3 times per week) between hypertensive and normotensive siblings. Hypertensive siblings were significantly less likely to be current smokers and significantly more likely to be former smokers than normotensive siblings. When the risk factors presented in Table 1 were summed for each sibling, those with hypertension were found to have a significantly higher mean number of risk factors (smoking, obesity, inactivity, high fat diet, hyperlipidemias) than those with normal BP (3.4 versus 2.9, $P$ = 0.0001).

### Awareness, Treatment, and Control

Among all hypertensive siblings (n = 380), 60% were aware, 45% were currently receiving pharmacological treatment, and 16% were under control. Differences by gender are shown in Figure 1. Control in siblings currently receiving antihypertensive therapy was 36% (n = 61 of 170).

Overall, hypertensive women were slightly but not significantly more likely to be aware of their hypertension (OR = 1.58, 95% CI = 0.96 to 2.61) and tended to be more likely to be receiving treatment in comparison with white siblings (OR = 1.32, 95% CI = 0.97 to 1.82).

African Americans were slightly but not significantly more likely to be aware of their hypertension (OR = 1.58, 95% CI = 0.96 to 2.61) and tended to be more likely to be receiving treatment in comparison with white siblings (OR = 1.32, 95% CI = 0.97 to 1.82).

### Table 1. Age-Adjusted Prevalence of CHD Risk Factors Among Siblings (n=859)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence Among Hypertensive* Siblings, % (n=380)</th>
<th>Prevalence Among Normotensive† Siblings, % (n=479)</th>
<th>$P$‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoking</td>
<td>29</td>
<td>36</td>
<td>0.029</td>
</tr>
<tr>
<td>Obesity</td>
<td>61</td>
<td>32</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Inadequate physical activity</td>
<td>84</td>
<td>82</td>
<td>0.58</td>
</tr>
<tr>
<td>High fat diet</td>
<td>82</td>
<td>81</td>
<td>0.77</td>
</tr>
<tr>
<td>Serum total cholesterol $\geq$ 5.17 mmol/L (200 mg/dL)</td>
<td>80</td>
<td>68</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglycerides $\geq$ 2.26 mmol/L (200 mg/dL)</td>
<td>28</td>
<td>15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL cholesterol $\geq$ 3.36 mmol/L (130 mg/dL)</td>
<td>72</td>
<td>65</td>
<td>0.03</td>
</tr>
<tr>
<td>HDL cholesterol $&lt;0.91$ mmol/L (35 mg/dL)</td>
<td>15</td>
<td>14</td>
<td>0.88</td>
</tr>
</tbody>
</table>

*Hypertensive is defined as BP $\geq$ 140/90 mm Hg and/or current antihypertensive pharmacotherapy.
†Normotensive is defined as BP $<140/90$ mm Hg with no antihypertensive pharmacotherapy.
‡Significance value for comparison of prevalences between hypertensive and normotensive siblings using the $\chi^2$ statistic.

## Figure 1

Awareness, treatment, and control among hypertensive siblings (n=380) by gender. *Hypertension is defined as BP $\geq$ 140/90 mm Hg and/or current antihypertensive pharmacotherapy.
CI=0.82 to 2.12), although this finding is not statistically significant.

Older persons (age 45 to 59 years) were somewhat more likely to be aware of their hypertension. There was a trend by decade (30 through 39, 40 through 49, or 50 through 59 years of age) for older persons also to be significantly more likely to be under treatment for their hypertension ($\chi^2$ for trend=6.85, $P=0.009$). Of those being treated, by decade, older persons were significantly more likely to be under control ($\chi^2$ for trend=4.59, $P=0.032$).

There were no differences in rates of awareness, treatment, or control by high school completion compared with less than a high school education.

### NHANES Comparison

To determine the validity of using NHANES III data for reference comparisons, the entire sibling sample was divided into 3 groups by time of screening: 1983 through 1987, pre-NHANES III; 1988 through 1991, during NHANES III (phase I); and 1992 through 1996, post-NHANES III (phase I). Mean SBP and DBP levels among all siblings from 1983 through 1987, 1988 through 1991, and 1992 through 1996 showed only very small decrements over time (systolic 134.7±16, 134.4±12, 132.1±16 mm Hg; diastolic 86.0±10, 85.5±9, 83.9±10 mm Hg, respectively). There were also no significant differences in the prevalence of hypertension or the categories of hypertension among siblings by these time periods.

Siblings experienced higher rates of hypertension than the NHANES III population, across race, gender, and age levels (Table 2) and all stages of hypertension (Figure 2). Awareness, treatment, and control of hypertension levels were consistently lower among siblings than in the NHANES III population (Figure 3) across race and gender levels (Table 3).

### Interventions

Few hypertensive siblings self-reported any lifestyle efforts to treat high BP. Analysis of a subsample in whom diet and physical activity were assessed showed that more than three quarters of those with hypertension were overweight and did not participate in any regular physical activity. Almost two thirds of those with hypertension were consuming $>2500$ mg/d sodium in foods alone, and the mean sodium consumption for hypertensive siblings was $2893±1007$ mg/d. Eleven percent of hypertensive siblings were consuming more than 10% of calories as alcohol. These measures of lifestyle were virtually the inverse of those reported by NHANES III participants, among whom more than three quarters of hypertensive individuals reported the use of 1 or more nonpharmacological or lifestyle therapies, as opposed to only one quarter of the hypertensive siblings in the present study.

Among those siblings who were being treated for hypertension with pharmacological agents (n=170), monotherapy
was far more common (72%) than combination therapy (28%). Diuretics were the most common agents used, both as monotherapy (35%) and as part of combination therapy (84%). There were no significant differences between monotherapy and combination therapy in control of hypertension.

Discussion

This study shows that siblings of persons who have had a premature CHD event are not adequately aware of, treated for, or controlled for hypertension. One possible reason for this poor awareness, self-care, and medical care is that siblings do not perceive themselves to be at risk for CHD events. Anecdotally, siblings in this study at the time of screening interviews quickly pointed out the ways in which they were different from the sibling who had the CHD event. Also, siblings often seemed interested in screening primarily to reassure themselves that they were not at risk.

The JNC-VI guidelines clearly extend the earlier mandate for prevention, early detection, and treatment of high BP. These new guidelines emphasize the importance of primary prevention and reinforce patient education and methods to improve patient compliance. They also provide physicians with very clear pathways for both lifestyle modification and pharmacological care. A family history of premature cardiovascular disease is again noted as a major factor in risk stratification and medical management. This study produces strong evidence that apparently healthy siblings of persons with premature coronary disease have a high prevalence of elevated BP levels and are not following lifestyle recommendations or receiving appropriate care for hypertension. Aggressive dissemination of these new guidelines will be necessary to create an impact on these high-risk families, as it appears that the prior guidelines have not been adequately applied to these individuals. As a recent JAMA article and editorial suggest, the JNC-VI guidelines may need to be disseminated on a wider scale to have any impact on physician practices.

Comparisons with national cross-sectional data still show the prevalence of awareness, treatment, and control of hypertension to be significantly lower among siblings than among the general population. Again, this indicates a need for greater awareness among providers about the uniquely high-risk status of persons in families with premature coronary disease.

From a familial-clustering and heritability perspective, it would have been interesting to observe BP differences between these siblings and a control group without a family history. However, the research question in this study was quite different. The purpose was to examine the deviation of apparently healthy siblings at high risk for premature CHD from national reference norms for BP.

A limitation of this study may be the exclusion of insulin-dependent diabetics, which may have resulted in an underestimate of the prevalence of hypertension and other CHD risk factors. Siblings were accrued over a period of 13 years. Depending on the time of their baseline examinations, they could have fallen into 1 of 4 JNC treatment recommendation sets. However, statistical tests showed no significant differences in prevalence of hypertension (P=0.611) or treatment of hypertension (P=0.397) when comparing siblings by which JNC report would have been in practice at the time of screening. Finally, the classification recommendations for BP screening were intended to be applied to measures of BP over multiple days. The screening process for siblings took place all in 1 day, so it was not possible to do this. To determine the extent to which multiple measurements on a single day may have produced an overestimation of high BP in comparison to the NHANES refersent in which multiple measures were accrued on different days, data from a 10% subsample of siblings who returned for a subsudy within 3 months of their initial screening showed a high correlation of BPs (SBP r=0.66; DBP r=0.70) and strong agreement for hypertension classification (κ=0.69, 95% CI=0.54 to 0.85). It is unlikely that the single-day measures produced sufficient bias to have influenced our conclusions.

**Conclusion**

Siblings of persons with premature CHD are a high-risk population with an increased prevalence of hypertension in combination with high levels of other modifiable CHD risk factors and inadequate levels of awareness, treatment, and control. Physician recommendations that promote lifestyle changes have a high probability of potentially lowering BP levels, as well as influencing concomitant risk factors, if persons are compliant. Given the inadequate levels of control among hypertensive siblings receiving therapy, pharmacological treatment may need to be more closely monitored and aggressively adapted to achieve optimal levels of BP. Siblings are an easily identifiable high-risk group who remain in...
need of improved screening and effective treatment strategies to lower rates of hypertension.

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