High-Normal Blood Pressure Progression to Hypertension in the Framingham Heart Study

Mark Leitschuh, L. Adrienne Cupples, William Kannel, David Gagnon, and Aram Chobanian

This study sought to determine if individuals with high-normal blood pressure (diastolic blood pressure of 85–89 mm Hg) progress to hypertension more frequently than those with normal blood pressure (diastolic blood pressure less than 85 mm Hg), thus advancing to a higher cardiovascular risk category. Individuals from the Framingham Heart Study were placed in normal and high-normal blood pressure categories and followed for 26 years for the development of hypertension. With hypertension defined as a diastolic blood pressure of 95 mm Hg or greater or the initiation of antihypertensive therapy, 23.6% of men and 36.2% of women with normal blood pressure developed hypertension compared with 54.2% of men and 60.6% of women with high-normal blood pressure. The relative risk for the development of hypertension associated with high-normal blood pressure was 2.25 for men (95% confidence interval [CI], 1.8–2.8; \( p < 0.0001 \)) and 1.89 for women (95% CI, 1.5–2.3; \( p < 0.0001 \)). The age-adjusted relative risks estimated by the proportional hazards model were 3.36 for men and 3.37 for women (\( p < 0.001 \)). Among those risk factors examined, baseline systolic and diastolic blood pressure, Metropolitan relative weight, and change in weight over time were significant predictors of future hypertension in men and women whose initial blood pressure was normal. For men with high-normal blood pressure, systolic blood pressure and change in weight were identified as risk factors for future hypertension. These results indicate that the probability of individuals with blood pressure in the high-normal range developing hypertension is twofold to threefold higher than in those with normal blood pressure. Therefore, we recommend that persons with high-normal blood pressure be followed up with frequent blood pressure testing and counseled on modification of risk factors. (Hypertension 1991;17:22–27)

In 1984, the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure introduced the concept of high-normal blood pressure, responding to concerns that even modest elevations in blood pressure previously considered normal may promote increased risk of premature cardiovascular morbidity and mortality.1 High-normal blood pressure was defined as a diastolic blood pressure of 85–89 mm Hg compared with the normal diastolic blood pressure of less than 85 mm Hg. Although definite cardiovascular risk is associated with this level of blood pressure,2 undetermined is whether the reduction in the blood pressure to the normal level would reduce this risk. One important factor would influence the decision of whether to reduce such modest blood pressure elevations to more optimal levels with nonpharmacological means: the possibility that individuals with high-normal blood pressure progress to hypertension at a greater rate than those with strictly normal blood pressure, thus advancing to a higher cardiovascular risk category that may indicate a need for treatment. If this process were to occur, then attempts to prevent this progression by modification of known risk factors for the development of hypertension would seem indicated. Therefore, we have used the 30-year follow-up data from the Framingham Heart Study to determine the rate of progression from high-normal blood pressure to hypertension compared with that of normal blood pressure; we also examined some possible risk factors associated with the development of hypertension in both groups.

Methods

The cohort of 5,209 men and women from the Framingham Heart Study were first examined be-
between 1949 and 1952 and have been followed up for 32 years with biennial exams. Each examination included extensive cardiovascular history and physical exam, an electrocardiogram, and two physician-measured blood pressure determinations. Systolic and fifth-phase diastolic blood pressure readings were taken from the left arm with a mercury sphygmomanometer with the subject seated. Data on the use of antihypertensive agents was gathered by interview of the subjects, starting with the fourth exam (1958–1960). Before that exam, few oral antihypertensive agents were available and hypertension was grossly undertreated.

Initial Categorization of Normal and High-Normal Blood Pressure

Individuals from the cohort were initially placed in normal and high-normal blood pressure categories, which were based on the average physician-measured blood pressures from the first three biennial exams. Normal blood pressure was defined as an average diastolic blood pressure of less than 85 mm Hg and a systolic blood pressure of less than 140 mm Hg. High-normal blood pressure was defined as an average diastolic blood pressure of 85–89 mm Hg and a systolic blood pressure of less than 140 mm Hg. Individuals excluded from categorization were those with the following conditions: 1) preexisting coronary heart disease, defined by clinical or electrocardiographic evidence of angina pectoris or myocardial infarction; 2) other preexisting cardiovascular disease, defined by evidence of claudication or cerebrovascular disease; 3) current or prior left ventricular hypertrophy on electrocardiogram; 4) cardiomegaly on chest radiograph; and 5) other conditions requiring antihypertensive medications. Individuals with preexisting coronary artery disease were excluded because of the possible effect of antianginal therapy or myocardial infarction on blood pressure. Those persons with cerebrovascular or other peripheral vascular disease were excluded because of the possible effect of such disease on accurate blood pressure measurement. Those individuals with cardiomegaly or left ventricular hypertrophy were excluded to eliminate persons with congestive heart failure or “burnt-out” severe hypertension who showed normal or high-normal blood pressure.

Development of Hypertension

The development of hypertension was determined in those individuals placed in high-normal and normal blood pressure categories at exam 3 and followed up for 26 years to exam 16. Those who died are included in the analysis up to the time of death. The analysis to determine the percentage of individuals who developed hypertension was conducted on two separate occasions by the use of two different blood pressures to define hypertension. First, hypertension was defined as a physician-measured diastolic blood pressure of 90 mm Hg or greater on two consecutive biennial exams or the initiation of antihypertensive therapy. To insure that significant increases in blood pressure had occurred in those who developed hypertension, we repeated the analysis, with 95 mm Hg as the cutoff level for defining hypertension. All further analyses, including those of risk factors, use the latter definition of hypertension.

Risk Factors for the Development of Hypertension

The following potential risk factors for the development of hypertension (diastolic blood pressure 95 mm Hg or greater) were averaged over exams 1–3 and evaluated: 1) Metropolitan relative weight (percentage), 2) glucose intolerance (diagnosis of diabetes mellitus, glucose in urine, or fasted blood glucose of greater than 120 mg/100 ml), 3) initial systolic blood pressure (mm Hg), 4) initial diastolic blood pressure (mm Hg), 5) vital capacity–height index (ml/in.), 6) fasting cholesterol (mg/100 ml), 7) hemoglobin (percentage), 8) cigarettes smoked (number/day), and 9) alcohol consumption (oz/mo). Alcohol consumption was determined by a single questionnaire during the interview of participants at their biennial exam, asking for the usual intake per week. Other risk factors, including family history of hypertension and dietary factors such as salt intake, which have been reported to be important in the development of hypertension, were not included in the initial data base of the Framingham Heart Study and consequently were not included in this analysis. Additionally, weight change from the average at exams 1, 2, and 3 to the weight at the exam in which hypertension was diagnosed was compared with the weight change for those in whom hypertension did not develop followed up for a similar time period (exam 9). The weight was expressed as the Quetelet index, which is defined as pounds per inch of height squared multiplied by 100. Comparison of the risk factors among those in whom hypertension developed and those in whom it did not was evaluated with the t (continuous measures) and χ² (categorical measures) tests and linear regression analysis to adjust for age at exam 3. Proportional hazards models were used to evaluate the multivariate relation between these measures and the development of hypertension.

Results

Initial Categorization of Blood Pressure and Progression to Hypertension

Table 1 shows the progression of normal and high-normal blood pressure to hypertension when hypertension was defined as a diastolic blood pressure of 90 mm Hg or greater or the initiation of antihypertensive therapy. Among those with normal blood pressure, hypertension developed in 33% of men and 42% of women compared with 71% of men and 78% of women with high-normal blood pressure. The relative risk for the development of hypertension associated with high-normal blood pressure was 2.1 for men (95% confidence interval, 1.8–2.5) and 1.9 for women (95% confidence interval, 1.6–2.3; p<0.0001 for both). Similar results were obtained.
when we used the definition of hypertension as a diastolic blood pressure of 95 mm Hg or higher or the initiation of antihypertensive therapy (Table 2). Although the number and percentage of hypertensive individuals was smaller, the relative risk associated with high-normal blood pressure was nearly the same. These results suggest that it is twice as probable that hypertension will develop in both men and women with high-normal blood pressure than in those with normal blood pressure.

Figures 1 and 2 plot the age-adjusted incidence of hypertension, which was estimated by the proportional hazards model for men and women. Both men and women with high-normal blood pressure have a higher incidence of hypertension compared with those with normal blood pressure. The age-adjusted risk for the development of hypertension was 3.36 for men and 3.37 for women by this form of analysis ($p<0.001$).

**Risk Factors for the Development of Hypertension**

Tables 3 and 4 show the age-adjusted means for those variables studied as potential risk factors for the development of hypertension in men and women with normal and high-normal blood pressure. For individuals with normal blood pressure, baseline systolic and diastolic blood pressure and Metropolitan relative weight for both men and women were statistically significant risk factors. For women only, serum cholesterol was also a significant predictor of future hypertension. For men only with high-normal blood pressure, diastolic blood pressure was a significant risk factor.

---

**TABLE 1.** Progression to Hypertension (Diastolic Blood Pressure 90 mm Hg or Greater) Over 26-Year Follow-up Period Based on Initial Blood Pressure, Sex, and 10-Year Age Groups

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Hypertensive n(%)</td>
</tr>
<tr>
<td><strong>Normal blood pressure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>205</td>
<td>78 (38.5%)</td>
</tr>
<tr>
<td>40–49</td>
<td>305</td>
<td>105 (34.4%)</td>
</tr>
<tr>
<td>50–59</td>
<td>172</td>
<td>47 (27.3%)</td>
</tr>
<tr>
<td>60–69</td>
<td>68</td>
<td>12 (27.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>750</td>
<td>249 (33.2%)</td>
</tr>
<tr>
<td><strong>High-normal blood pressure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>40</td>
<td>31 (77.5%)</td>
</tr>
<tr>
<td>40–49</td>
<td>71</td>
<td>54 (76.1%)</td>
</tr>
<tr>
<td>50–59</td>
<td>39</td>
<td>22 (56.4%)</td>
</tr>
<tr>
<td>60–69</td>
<td>3</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>108 (70.6%)*</td>
</tr>
</tbody>
</table>

Normal blood pressure, diastolic blood pressure less than 85 mm Hg and systolic blood pressure less than 140 mm Hg; high-normal blood pressure, diastolic blood pressure of 85–89 mm Hg and systolic blood pressure less than 140 mm Hg.

*Mantel-Haenzel relative risk, 2.11; 95% confidence interval, 1.81-2.50; $p<0.0001$.

†Mantel-Haenzel relative risk, 1.90; 95% confidence interval, 1.60-2.30; $p<0.0001$.

---

**TABLE 2.** Progression to Hypertension (Diastolic Blood Pressure 95 mm Hg or Greater) Over 26-Year Follow-up Period Based on Initial Blood Pressure, Sex, and 10-Year Age Groups

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Hypertensive n(%)</td>
</tr>
<tr>
<td><strong>Normal blood pressure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>205</td>
<td>51 (24.9%)</td>
</tr>
<tr>
<td>40–49</td>
<td>305</td>
<td>78 (25.6%)</td>
</tr>
<tr>
<td>50–59</td>
<td>172</td>
<td>36 (20.9%)</td>
</tr>
<tr>
<td>60–69</td>
<td>68</td>
<td>12 (17.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>750</td>
<td>177 (23.6%)</td>
</tr>
<tr>
<td><strong>High-normal blood pressure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>40</td>
<td>19 (47.5%)</td>
</tr>
<tr>
<td>40–49</td>
<td>71</td>
<td>47 (66.2%)</td>
</tr>
<tr>
<td>50–59</td>
<td>39</td>
<td>16 (41.0%)</td>
</tr>
<tr>
<td>60–69</td>
<td>3</td>
<td>1 (33.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>83 (54.2%)*</td>
</tr>
</tbody>
</table>

Normal blood pressure, diastolic blood pressure less than 85 mm Hg and systolic blood pressure less than 140 mm Hg; high-normal blood pressure, diastolic blood pressure of 85–89 mm Hg and systolic blood pressure less than 140 mm Hg.

*Mantel-Haenzel relative risk, 2.25; 95% confidence interval, 1.81-2.79; $p<0.001$.

†Mantel-Haenzel relative risk, 1.89; 95% confidence interval, 1.60-2.30; $p<0.0001$. 

Downloaded from http://hyper.ahajournals.org/ on October 16, 2017
Multivariate Cox regression analyses confirmed that initial systolic and diastolic blood pressure were predictors of hypertension in men and women whose initial blood pressure was normal (p<0.001). Systolic blood pressure in men and diastolic blood pressure in women with high-normal blood pressure were also significant. If one eliminates from the analysis the powerful effect of blood pressure, the Metropolitan relative weight is seen to be an independent predictor of hypertension (p<0.05). As shown in Table 5, a 10% increase in Metropolitan relative weight confers an approximate 20–25% increased risk for the development of hypertension.

Figure 3 presents the results of an analysis done to determine if a change in weight over time might be a significant risk factor for the development of hypertension. Men with normal and high-normal blood pressure and women with normal blood pressure in whom hypertension developed had a statistically significant gain in weight compared with those in whom it did not develop. Hypertension developed in women with high-normal blood pressure who also gained weight, but this correlation failed to reach statistical significance, possibly because of the relatively small number of individuals in the group. Those in whom hypertension did not develop, despite high-normal blood pressure, demonstrated a significant loss of weight.

**Discussion**

The primary objective of this study was to determine if individuals with high-normal blood pressure progress to hypertension at a greater rate than those with strictly normal blood pressure. We have shown that it is at least twofold more probable for hypertension to develop in individuals with high-normal blood pressure than in those with normal blood pressure. These results confirm previous studies that have found the level of initial blood pressure to be predictive of the development of hypertension but more clearly define the risk for the specific group of individuals with high-normal blood pressure.3-9

The analysis of potential risk factors for the development of hypertension discloses the importance of systolic and diastolic blood pressure as predisposing factors for both men and women with normal blood pressure. For men with high-normal blood pressure, only diastolic blood pressure was significant. Mean relative weight for men and women and serum cholesterol level for women with normal blood pressure were also statistically significant contributors. If one compares the normal with the high-normal group,
persons with high-normal blood pressure are seen to have higher Metropolitan relative weights than those with normal blood pressure. As shown in Figure 3, the weight change over time also appears to be important for the prediction of hypertension. Individuals who became hypertensive gained more weight than those who remained normotensive. This factor failed to reach statistical significance for women with high-normal blood pressure, perhaps because the number in this group was small. Concomitantly, these data would suggest that weight loss in those above optimum desirable weight and avoidance of weight gain are important in the prevention of hypertension.

Previous studies have suggested that alcohol consumption may contribute to the development of hypertension, but individuals must consume a relatively large amount of alcohol every day for this to occur. In the total Framingham cohort, no increase was seen in the incidence of hypertension until more than 29 ounces of alcohol each month was consumed. In this subset of the cohort, alcohol consumption was modest (men, 19–24 oz/mo; women, 7–8 oz/mo), which may be why we failed to identify it as a predictor of hypertension. Finally, because alcohol consumption was determined by questionnaire and had no independent validation, these results are less reliable than those risk factors that were actually measured.

A number of limitations of this study should be considered while interpreting the results. Not all risk factors now considered important in the development of hypertension were initially included in the Framingham Heart Study; therefore, they were not included in this analysis. This omission also holds for nutritional factors such as salt intake. Results from the INTERSALT study showed that sodium excretion was significantly and independently related to systolic blood pressure. In terms of this relation, Stamler has estimated that a reduction in the population sodium intake of 100 mmol/day would result in an average population systolic blood pressure that was at least 2.2 mm Hg lower. In addition, the Framingham population consisted of primarily white, middle-class individuals with an underrepresentation of different minority and socioeconomic groups. Also, the number of individuals in the older age groups was small, especially in the high-normal blood pressure group. Because of these limitations, the results and recommendations of the study should be considered with caution when applied to elderly and minority subjects.

An important question arises from the findings of this study. Is the progression from high-normal blood pressure to hypertension preventable without exposure of this large population to the risks and cost of
pharmacological antihypertensive therapy? Two recent clinical trials have reported the ability to prevent the development of hypertension in individuals with normal or high-normal blood pressure by dietary or hygienic means. In the Primary Prevention of Hypertension study,13 individuals who were prone to hypertension (i.e., those who had high-normal blood pressure [first-screen diastolic blood pressure of 80–89 mm Hg with a second-screen value of 85–89 mm Hg]) or had normal blood pressure (80–89 mm Hg) with obesity or a rapid pulse rate were randomly assigned to an intervention or control group. The goals of intervention were a reduction in weight with a fat-modified, American Heart Association-type diet, reduction in daily sodium intake and alcohol consumption, and an increase in physical activity. The incidence of hypertension over the 5-year trial was 8.8% for the intervention group and 19.2% for the control group (odds ratio, 2.4). In the Hypertension Prevention Trial,14 841 men and women with diastolic blood pressures of 76–89 mm Hg were randomly assigned to a control treatment group or one of four dietary counseling groups (reduced calories, sodium, sodium and calories, or reduced sodium and increased potassium). In all treatment groups, blood pressure decreased below the level of controls. These results indicate the feasibility of preventing the progression to hypertension by nonpharmacological means, but further study is needed to determine the benefits of such intervention.

In summary, we have provided specific epidemiological information regarding the risk of hypertension for individuals with high-normal blood pressure. Recent trials have suggested the feasibility of preventing the development of hypertension by nonpharmacological means, and further trials seem warranted to determine the benefits of such interventions in the prevention of cardiovascular morbidity and mortality.

**References**

7. Svardsudd K, Wedel H, Wilhelmsen L: Factors associated with the initial blood pressure level and with subsequent blood pressure increase in a longitudinal population study. Eur Heart J 1980;1:345–354

**Key Words** — blood pressure • essential hypertension • risk factors
High-normal blood pressure progression to hypertension in the Framingham Heart Study.
M Leitschuh, L A Cupples, W Kannel, D Gagnon and A Chobanian

Hypertension. 1991;17:22-27
doi: 10.1161/01.HYP.17.1.22
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1991 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/17/1/22

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in
Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located, click
Request Permissions in the middle column of the Web page under Services. Further information about this
process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/