The Prognosis of Hypertension According to Age at Onset

CAROL BUCK, PEGGY BAKER, MARTIN BASS, AND ALLAN DONNER

SUMMARY Data from a program for hypertension screening and follow-up were used to study the relationship between age at onset of hypertension and the risk of cardiovascular complications. The risk for hypertensive subjects, compared with normotensive subjects of similar age, declined significantly as age of onset increased from 40 to 69 years. This pattern was not explained by differences in initial severity of hypertension, control of hypertension, obesity, smoking, or alcohol consumption. A sex-specific analysis showed that the pattern was confined to male subjects, but it is argued that it might be seen in female subjects if data for women of more advanced age were available. Further lines of investigation of this interesting phenomenon are proposed. (Hypertension 9: 204-208, 1987)

KEY WORDS • hypertension • prognosis • age • geriatrics

It is well established that hypertension in the elderly is significantly related to cardiovascular morbidity and mortality. What is not known is the prognosis of hypertension that begins in old age. Framingham study observations of cardiovascular disease after age 65 years show a positive correlation between the number of years of elevated systolic pressure before age 65 years and the risk of disease thereafter. These observations do not, however, allow a distinction to be made between age at onset and duration of hypertension.

We have had an opportunity to examine the question by comparing the risk of cardiovascular disease among inception cohorts of hypertensive subjects according to their age at onset of hypertension.

Subjects and Methods
From 1978 to 1982, 34 general practices in southwestern Ontario took part in a trial of a system for improved detection and management of hypertension. During this 5-year period, both fatal and nonfatal cardiovascular events were recorded for all patients aged 20 to 69 years. The events included myocardial infarction, stroke, congestive heart failure, and renal failure (see Appendix at end of text).

To investigate the relationship between age at onset of hypertension and the risk of cardiovascular events, we compared event rates among newly diagnosed hypertensive patients with rates among normotensive subjects of comparable age. Three cohorts of newly diagnosed hypertensive subjects who were aged 40 to 49, 50 to 59, and 60 to 65 years at the beginning of the 5-year period of observation were compared with normotensive cohorts in the same age groups at baseline (1978). The diagnosis of hypertension was made on the basis of a diastolic pressure of 90 mm Hg or greater on two consecutive office visits. The purpose of the study was to examine the effect of age at onset of hypertension, rather than that of age at diagnosis. Therefore, we included only the newly diagnosed hypertensive patients whose charts showed at least one previous normotensive blood pressure, no elevated pressures, and no record of treatment for hypertension in the 5-year period before baseline.

In computing the rates of cardiovascular events, we included in the denominators subjects who were lost to follow-up because they had moved or had died of a noncardiovascular event. Among the hypertensive subjects, the percentages lost to follow-up were 3.8, 5.6, and 5.9 at ages 40 to 49, 50 to 59, and 60 to 65 years, respectively. Among the corresponding cohorts of normotensive subjects, the percentages were 10.2, 12.3, and 14.6. Because of these inequalities the extent of withdrawal bias was estimated, first by excluding the lost to follow-up subjects from the denominators, and second by making extreme assumptions about event rates among the lost to follow-up subjects.

Although the diagnosis of hypertension could have
been made at any time during the period from 1978 to 1982, in computing event rates we considered the hypertensive subjects to have been at risk for the whole 5-year period. The potential bias introduced by this procedure will be discussed later.

### Results

Table 1 shows the rates of cardiovascular events for each hypertensive cohort and the corresponding normotensive comparison group. The excess risk associated with hypertension declined sharply from the youngest to the oldest age groups, and the test of homogeneity among the odds ratios showed this trend to be statistically significant. Recalculation of the rates with withdrawals excluded, or with the assumption made that all the older hypertensive withdrawals had had events, did not remove the age gradient in the odds ratios. A similar gradient was found for each type of cardiovascular event: stroke, myocardial infarction, and congestive heart failure.

The next step was to examine the three hypertensive cohorts in terms of the severity of their hypertension at the time of diagnosis. Table 2 gives the mean blood pressure (pretreatment) for hypertensive and for normotensive subjects, and the mean difference in systolic and diastolic pressure between each hypertensive cohort and its normotensive counterpart. The degree of elevation of pressure in the hypertensive subjects as compared with the normotensive subjects was comparable in the three age-at-onset cohorts.

The adequacy of blood pressure control was compared among the age-at-onset cohorts. Adequate control was defined as a mean diastolic pressure less than 90 mm Hg over all blood pressures measured after the diagnosis of hypertension. Table 3 shows that the proportion of patients with adequate blood pressure control declined slightly with age at onset. Therefore, the better prognosis of late-onset subjects cannot be ascribed to better control of blood pressure.

The next step was to compare the hypertensive cohorts with their normotensive comparison groups in terms of three important risk factors for cardiovascular events: obesity, cigarette smoking, and alcohol consumption. Obesity was defined in terms of a body mass index greater than 25 for women and greater than 27 for men. For the smoking variable, subjects were dichotomized according to whether they had ever smoked cigarettes. This grouping was more appropriate than categorizing them according to their current smoking habits, since some hypertensive subjects had stopped smoking at the time their hypertension was diagnosed. For alcohol consumption, subjects who reported that they did not use alcohol were separated from all others. This dichotomy was based on our observation that the occurrence of cardiovascular events was higher among nondrinkers than among drinkers, whatever the level of consumption among the latter. Table 4 presents a comparison of hypertensive with normotensive subjects in each age group for the three potentially confounding variables. It shows that the differences did not, in general, favor the oldest cohort. Nevertheless, a further analysis to allow for potential confounding was performed. To formally test whether the heterogeneity among the odds ratios (presented in Table 1) persisted after adjusting for smoking, alcohol consumption, and obesity, a two-degree-of-freedom likelihood ratio test was performed using multiple logistic regression. For this analysis, indicator variables were defined to represent hypertensive status (hypertensive vs normotensive subjects), age group at onset (40–49, 50–59, 60–65 years), and the

### Table 1. Five-Year Occurrence of Cardiovascular Events in Newly Diagnosed Hypertensive Subjects and Normotensive Subjects by Age at Baseline

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>New hypertensive</th>
<th>Normotensive</th>
<th>Odds ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>4.6 (239)</td>
<td>0.9 (4677)</td>
<td>5.2</td>
</tr>
<tr>
<td>50–59</td>
<td>5.6 (288)</td>
<td>3.2 (3655)</td>
<td>1.8</td>
</tr>
<tr>
<td>60–65</td>
<td>6.5 (153)</td>
<td>5.7 (1301)</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Number of subjects shown in parentheses.

*Test of homogeneity among the odds ratios: $\chi^2 = 10.14, df = 2, p < 0.01$.

### Table 2. Mean Blood Pressure of Newly Diagnosed Hypertensive Subjects* and Normotensive Subjects

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>New hypertensive</th>
<th>Normotensive</th>
<th>Between-group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SBP (mm Hg)</td>
<td>DBP (mm Hg)</td>
<td>SBP (mm Hg)</td>
</tr>
<tr>
<td>40–49</td>
<td>149.8</td>
<td>95.9</td>
<td>122.4</td>
</tr>
<tr>
<td>50–59</td>
<td>155.2</td>
<td>96.2</td>
<td>126.7</td>
</tr>
<tr>
<td>60–65</td>
<td>162.2</td>
<td>95.8</td>
<td>132.1</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; DBP = diastolic blood pressure.

*Pretreatment blood pressure.
three potential confounders. Two models were fitted, including and excluding the interaction terms of age group with hypertensive status. The results are displayed in Table 5. The difference in $-2$ (log likelihood) between the two models is distributed as a chi square with two degrees of freedom under the null hypothesis that the three adjusted odds ratios are homogeneous. The test yielded $\chi^2$ of 8.08 ($p = 0.02$). Thus, the more favorable prognosis of late-onset hypertension cannot be ascribed to confounding by smoking, alcohol consumption, or obesity.

Another risk factor that might have been confounded with age at onset of hypertension is the serum lipid profile. Although our source of data did not provide such information for normotensive subjects, we had lipid profiles for hypertensive subjects whose physicians included serum lipids in their diagnostic investigation. Table 6 presents a comparison of total serum cholesterol and the ratio of high density to low density lipoprotein cholesterol among age-at-onset cohorts from this subgroup of newly diagnosed hypertensive subjects. The differences by age at onset were small and did not favor the oldest cohort. This observation does not entirely rule out the possibility of confounding. Because the hypertensive cohorts were compared with their normotensive counterparts, one must consider the possibility of differences among the latter in serum lipids. If the oldest normotensive subjects had a more unfavorable lipid profile compared with the oldest hypertensive subjects, the observed advantage of the latter could have arisen from such a discrepancy. Although this remains a possibility, there is no a priori reason for assuming that the lipid profile would vary with age more among normotensive subjects than among newly diagnosed hypertensive subjects.

Because the cohorts were designated by broad 10-year age groups, the results could have been caused by an age bias. Therefore, we computed the mean age at baseline for each hypertensive and normotensive cohort. The hypertensive and normotensive cohorts were almost identical in mean age in each of the three comparison groups.

In the description of the methods, we mentioned that newly diagnosed hypertensive subjects were considered to be at risk of a cardiovascular event throughout the period from 1978 to 1982, regardless of the year in which the diagnosis of hypertension was made. This could have introduced a bias capable of producing the observed results if the duration of hypertension systematically differed in the three hypertensive cohorts. This possibility was examined, and the results are shown in Table 7. No trend toward a shorter duration of hypertension with increasing age at onset was observed.

Finally, the effect of age at onset of hypertension was examined separately for men and women. The results are shown in Table 8. The pattern of a diminish-
ing excess risk from the youngest to the oldest hypertensive cohort was found for men, but to a much lesser extent for women (p < 0.005 for men and p > 0.50 for women).

**Discussion**

Although several important confounding variables have been eliminated, we did not have information on Type A and B behavior patterns nor on diabetes. It is conceivable that early-onset hypertension is associated with Type A behavior, but this seems unlikely in view of the overall lack of association between hypertension and Type A behavior.3 Diabetes could have contributed to the phenomenon that we have observed if the excess prevalence of diabetes among hypertensive subjects compared with normotensive subjects diminishes with age. Data for men aged 50 to 79 years from a California community study showed that this was the case among established hypertensive subjects, but information was not given for newly diagnosed elderly hypertensive subjects.4 Further studies of age at onset in relation to the prognosis of hypertension should take account of Type A and B behavior and diabetes.

Since most of the hypertensive subjects were receiving antihypertensive medication, it is difficult to know whether the apparently lower risk of cardiovascular sequelae reflects an inherently better prognosis in late-onset hypertension or whether the control of blood pressure is more effective in preventing complications in late-onset hypertension. Therefore, it is important to determine whether the pattern that we have observed is found also among untreated mild hypertensive subjects.

If late-onset hypertension has an inherently better prognosis or a greater benefit from treatment, what might be the mechanism? Hypertension is known to be heterogeneous in its physiological determinants. Cardiac output, peripheral vascular resistance, baroreceptor activity, the renin-angiotensin system, and the adrenergic system all play a part. It is possible that the cardiovascular consequences of hypertension differ according to the physiological mechanisms responsible for the development of high blood pressure. If this is so, a difference in the determinants of hypertension in middle age and old age might account for the better prognosis of late-onset hypertension. Physiological observations in hypertensive subjects of different ages have shown differences in cardiac output, heart rate, plasma renin activity, and peripheral resistance.7,8 The studies from which these observations come do not, however, permit a comparison of the physiological characteristics of hypertension according to age at onset. Our results indicate that such a comparison would be very important.
One could argue that it is not necessary to postulate that late-onset hypertension has different physiological determinants. This argument would arise from looking at Table 1 in a different way and noting that the diminished excess risk of cardiovascular events among the older hypertensive subjects was a result of the steeper age gradient in the rate of events among normotensive than among hypertensive subjects. Looking at it this way, one could simply conclude that age overtakes hypertension as a cause of cardiovascular disease. Here again, the importance of studying the physiology of late-onset hypertension becomes evident. Is late-onset hypertension a different entity?

The reduced risk of cardiovascular events associated with late-onset hypertension was found for men, but to only a slight degree for women. Sex differences in the determinants of disease outcome are common, and many of them remain unexplained. In this instance, a tentative explanation can be advanced. Measurements of blood pressure in population samples show that pressures are higher in men than in women before the age of 55 years but that the blood pressure of women equals or overtakes that of men beyond this age. If the development of hypertension in women is slower than that in men, late-onset hypertension for women might better be defined as hypertension beginning after the age of 65 years. Since our data provided no information for subjects beyond age 65 years at baseline, we cannot be certain that the phenomenon we have observed is restricted to men.

The importance of hypertension in the elderly is currently a subject of great interest, but the debate has not made a distinction between hypertension in the elderly and hypertension beginning in the elderly. Our results suggest that this distinction could be important. Furthermore, the frequency of late-onset hypertension is not negligible. In our hypertensive subjects with onset between the ages of 40 and 69 years, 20% had their onset at age 60 years or beyond.

References
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