Relationship of Blood Pressure to 25-Year Mortality Due to Coronary Heart Disease, Cardiovascular Diseases, and All Causes in Young Adult Men

The Chicago Heart Association Detection Project in Industry

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Background: Data are limited on blood pressure (BP) in young adults and long-term mortality. Moreover, screening and hypertension treatment guidelines have been based mainly on findings for middle-aged and older populations. This study assesses relationships of BP measured in young adult men to long-term mortality due to coronary heart disease (CHD), cardiovascular diseases (CVD), and all causes.

Methods: This cohort from the Chicago Heart Association Detection Project in Industry included 10,874 men aged 18 to 39 years at baseline (1967-1973), not receiving antihypertensive drugs, and without CHD or diabetes. Relationship of baseline BP to 25-year CHD, CVD, and all-cause mortality was assessed.

Results: Age-adjusted association of systolic BP to CHD mortality was continuous and graded. Multivariate-adjusted CHD hazard ratios (HRs) for 1 SD higher systolic BP (15 mm Hg) and diastolic BP (10 mm Hg) were 1.26 (95% confidence interval [CI], 1.11-1.44) and 1.17 (95% CI, 1.01-1.35), respectively. Compared with the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure stratum with normal BP (and lowest mortality rates), the large strata with high-normal BP and stage 1 hypertension had 25-year absolute risks for death of 63 and 72 per 1000, respectively, and absolute excess risks of 10 and 20 per 1000, respectively; accounted for 59.8% of all excess CHD, CVD, and all-cause mortality; and were estimated to have life expectancy shortened by 2.2 and 4.1 years, respectively.

Conclusions: In young adult men, BP above normal was significantly related to increased long-term mortality due to CHD, CVD, and all causes. Population-wide primary prevention, early detection, and control of higher BP are indicated from young adulthood on.
MATERIALS AND METHODS

POPULATION

Methods of the CHA study have been described. Briefly, 39,573 men and women aged 18 years and older underwent screening from November 1967 through January 1973. All employees at 84 cooperating Chicago-area companies and organizations, with a labor force of approximately 75,000 people, were invited to participate; volunteer rate was 53%.

SURVEY METHODS

Screening was performed by 2 trained and standardized 4-person field teams. Data collected at baseline included age, sex, ethnicity, education, BP, serum total cholesterol level, smoking status, height and weight, resting electrocardiographic (ECG) findings, medical history, and current treatment for chronic diseases, including hypertension and diabetes. A single casual supine BP measurement was obtained by trained staff using a standard mercury sphygmomanometer. Standardized high-quality methods were used for determination of total serum cholesterol levels. Criteria of the National Cooperative Pooling Project and the Hypertension Detection and Follow-up Program were used to code ECG abnormalities.

MORTALITY END POINTS

Vital status was ascertained through 1995, with average follow-up of 25 years. Deaths were determined before and including 1979 by means of direct mail, telephone, contact with employer, and matching of cohort records with Social Security Administration files, and after 1979 by means of matching of study records with National Death Index records. Multiple causes of death from death certificates were coded by trained research staff according to the International Classification of Diseases, Eighth Revision (ICD-8). Coding decisions were cross-checked by study team members. All coders were blinded to baseline data. For this report, underlying cause of death was used. Mortality due to CHD was defined as ICD-8 codes 410.0 to 414.9; that due to CVD, ICD-8 codes 150.2 to 445.9.

EXCLUSIONS

Men aged 18 to 39 years at baseline numbered 11,248. Of these, 374 were excluded for the following reasons: data missing at baseline or on follow-up (n=114); baseline ECG evidence of myocardial infarction (n=5); history of myocardial infarction or other CHD (n=12); antihypertensive drug treatment at baseline (n=125); or previously diagnosed diabetes mellitus (n=118). Thus, this report is based on 10,874 men.

STATISTICAL ANALYSES

Age-adjusted mortality rates per 10,000 person-years of follow-up and per 1000 men were computed for CHD, CVD, and all-cause mortality. Mortality rates were calculated by categories of SBP or DBP and by the following classification according to the JNC-VI: optimal (SBP of <120 mm Hg and DBP of <80 mm Hg); normal not optimal (SBP of 120-129 mm Hg and DBP of <85 mm Hg, or SBP of <130 mm Hg and DBP of 80-84 mm Hg); high normal (SBP of 130-139 mm Hg and DBP of <90 mm Hg, or SBP of 140 mm Hg and DBP of 85-89 mm Hg); stage 1 hypertension (SBP of 140-159 mm Hg and DBP of <100 mm Hg, or SBP of 160 mm Hg and DBP of 90-99 mm Hg); stage 2 hypertension (SBP of 160-179 mm Hg and DBP of <110 mm Hg, or SBP of <180 mm Hg and DBP of 100-109 mm Hg); and stage 3 hypertension (SBP of ≥180 mm Hg or DBP of ≥110 mm Hg). Rates were age adjusted by the direct method to the overall cohort age distribution.

Cox proportional hazards regression was used to calculate multivariate-adjusted hazard ratios (HRs) for death and their 95% confidence intervals (CIs) for baseline BP categories, and to obtain multivariate-adjusted coefficients for the relation of BP to mortality. The HRs were adjusted for age (years), race (African American or not), education (years), serum total cholesterol level (millimoles per liter [milligrams per deciliter]), cigarette smoking (cigarettes/day), body mass index (BMI) (weight in kilograms divided by square of height in meters), BMI2, and any ECG abnormality (no or yes).

Absolute excess death rates per 1000 in 25 years by JNC-VI stratum were calculated from age-adjusted mortality rates per 1000 in 25 years. The reference group was the stratum with normal (not optimal) BP. Numbers of excess deaths for other JNC-VI strata were calculated from these absolute excess rates and numbers of men in these strata. Percentage of all excess deaths in each stratum was also calculated.

Cox multivariate proportional hazards regression coefficients for the relation of JNC-VI strata to all-cause mortality were used to estimate years of shorter life expectancy for men with higher baseline BP levels compared with men with normal BP. Detailed methods for these calculations have been described elsewhere.

RESULTS

BASELINE FINDINGS

Table 1 presents data on baseline variables. At baseline, 8.6% of the cohort had optimal BP (JNC-VI criteria); 20.2%, normal (not optimal) BP; 25.5%, high-normal BP; and 36.4%, stage 1 hypertension.

BASELINE SBP AND DBP AND MORTALITY

During follow-up, 197 men died of CHD; 257 of CVD; and 759 of all causes.

Age-Adjusted Mortality Rates

With higher SBP, age-adjusted mortality due to CHD and CVD increased continuously and markedly (Table 2). For DBP, mortality due to CHD and CVD was lower for
men with DBP of 70 to 79 mm Hg than for those with DBP of less than 70 mm Hg. For strata with DBP of greater than 70 to 79 mm Hg, mortality rates were progressively and markedly higher.

For all-cause mortality, rates were lowest in men with SBP of 120 to 129 mm Hg and with DBP of 70 to 79 mm Hg; for strata with higher levels, rates were generally progressively higher.

Multivariate-Adjusted HRs

With SBP of 120 to 129 mm Hg and DBP of 70 to 79 mm Hg as the references, HRs for CHD, CVD, and all-cause mortality generally increased with higher SBP and DBP level (Table 2).

For men with DBP of less than 70 mm Hg, HRs were nonsignificantly higher for all 3 end points (1.63, 1.32, and 1.22 for CHD, CVD, and all-cause mortality, respectively) compared with men with DBP of 70 to 79 mm Hg.

Cox Multivariate-Adjusted Coefficients

For SBP and DBP, Cox coefficients were statistically significant for all 3 mortality end points (Table 2). For CHD deaths, these coefficients yielded HRs—for 1-SD higher SBP (15.2 mm Hg) and DBP (10.4 mm Hg)—of 1.26 (95% CI, 1.11-1.44) for SBP and 1.17 (95% CI, 1.01-1.35) for DBP. For comparison, these estimates for the CHA cohort of middle-aged men (aged 40-59 years) were 1.23 (95% CI, 1.15-1.32) for SBP and 1.29 (95% CI, 1.21-1.38) for DBP (coefficients 0.0108 and 0.0223; 1 SD, 19.3 mm Hg and 11.5 mm Hg).

BASELINE SBP/DBP (JNC-VI CRITERIA) AND LONG-TERM MORTALITY

Overall Findings

Age-adjusted death rates and multivariate-adjusted HRs were lowest for the normal (but not optimal) stratum (Table 3). Adjusted rates and HRs increased progressively for strata above normal BP, eg, CHD HRs of 1.37 for the high-normal stratum and of 1.62, 2.51, and 3.60 for hypertension stages 1, 2, and 3 strata, respectively, compared with the normal stratum.

HRs in Men With Optimal BP

For men with optimal BP, risks were relatively (nonsignificantly) higher for CHD, CVD, and all causes than for those with normal BP (Table 3). As mentioned in JNC-V and JNC-VI guidelines on optimal BP, unusually low BP readings need clinical evaluation.20,28 For men with optimal BP in this cohort, 45 deaths (of 59 due to all causes) were in the sizable high-normal stratum (2773 men), more than the small stratum (161 men) with stage 3 hypertension (Table 6). Of all excess deaths, 15.6% to 16.9% was in the large stratum (3963 of the 10874 men) with stage 1 hypertension, estimated life expectancy was longer by 2.2, 4.1, 8.4, and 12.2 years, respectively, compared with men with normal BP (25.5%+36.4%). These findings almost certainly reflect 1.24 (all causes). With exclusion also of men with DBP of 60 to 64 mm Hg, HR for all causes was reduced to 1.15 (95% CI, 0.79-1.68) (detailed data not shown).

ABSOLUTE EXCESS RISKS AND EXCESS DEATHS BY JNC-VI BP CLASSIFICATION

Absolute excess risks for CVD death were 6.3, 10.8, 33.1, and 74.1 per 1000 in 25 years for men with high-normal BP and stages 1, 2, and 3 hypertension, respectively (Table 6). For all-cause death, absolute excess risks ranged from 10.1 to 107.6 per 1000 in 25 years. For men with higher BP levels, ie, high-normal BP and stages 1, 2, and 3 hypertension, estimated life expectancy was shorter by 2.2, 4.1, 8.4, and 12.2 years, respectively, compared with men with normal BP.23,27

For each mortality end point, the highest proportion of all excess deaths—41.6% to 45.6%—was in the large stratum (3963 of the 10874 men) with stage 1 hypertension (Table 6). Of all excess deaths, 15.6% to 16.9% were in the sizable high-normal stratum (2773 men), more than in the small stratum (161 men) with stage 3 hypertension. Together, the high-normal and stage 1 hypertensive strata accounted for 58.5% of excess CVD deaths and 59.4% of excess deaths due to all causes.

COMMENT

The main findings on this cohort of young adult employed men are as follows. (1) Even at their age (average, 30 years), SBP/DBP at optimal or normal levels prevailed in only 28.8% (8.6%+20.2%), whereas (2) SBP/DBP was high-normal or stage 1 hypertension in 61.9% (25.5%+36.4%). These findings almost certainly reflect...
Cardiovascular Diseases

The adverse impact of dietary and other lifestyle traits leading to BP rise from youth onward in most people (eg, on average the cohort was overweight [BMI, 26.0]). (3) Blood pressure measured in young adulthood predicted long-term risks for CHD, CVD, and all-cause mortality. As in middle-aged and older persons,1-6 relationships of SBP, DBP, and other factors to future risk are strong, independent, and consistent across all age and risk strata. The increases in DBP seen with age are consistent, whether in high-normal or stage 1 hypertension. The evidence for DBP is consistent with that for SBP. The adverse impact of dietary and other lifestyle traits leading to BP rise from youth onward in most people (eg, on average the cohort was overweight [BMI, 26.0]). (3) Blood pressure measured in young adulthood predicted long-term risks for CHD, CVD, and all-cause mortality. As in middle-aged and older persons,1-6 relationships of SBP,
DBP, and SBP/DBP (JNC-VI strata) to mortality were generally graded, strong, and independent. (4) Multivariate-adjusted HRs tended to be greater for SBP than DBP, and similar in size to those for middle-aged men. (5) For the 2 large strata with high-normal BP and stage 1 hypertensive, 25-year absolute risks and absolute excess risks for mortality—for the years from average ages of 30 to 55 years—were substantial, eg, all-cause mortality rates of 63 and 72 per 1000 and absolute excess rates of 10 and 20 per 1000, translating into estimated shorter life expectancy of 2.2 and 4.1 years. These 2 strata accounted for 59.4% of all excess deaths attributable to above-normal SBP/DBP.

Observations on BP and CHD or total CVD mortality in young adults are limited, mainly because elucidation of this matter requires large sample sizes and long-term follow-up to accrue sufficient events for statistical analysis. In the 1960s, Paffenbarger et al. reported few previous findings and constitute, to our knowledge, the first detailed report from a large, long-term study of young adults from the general population showing a significant independent association of BP level and CHD or total CVD mortality.

Advanced coronary atherosclerosis was seen in most young American men undergoing autopsy during the Korean and Vietnam wars. Other studies of the natural history of atherosclerosis indicate that in populations with high rates of premature coronary artery disease, advanced lesions appear with increasing frequency during the years of childhood and young adulthood. In autopsy studies from the Bogalusa Heart Study, among children and young adults who died prematurely of noncardiac causes, the extent of involvement of aortic and coronary artery wall with fatty streaks and fibrous plaques was associated with major coronary risk factors, includ-

### Table 4. Underlying Cause for 45 Noncardiovascular Deaths With Optimal Blood Pressure at Baseline

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious diseases*</td>
<td>5 (11.1)</td>
</tr>
<tr>
<td>Acquired immunodeficiency syndrome</td>
<td>5 (11.1)</td>
</tr>
<tr>
<td>Neoplasms†</td>
<td>23 (51.1)</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>3 (6.7)</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>8 (17.8)</td>
</tr>
<tr>
<td>Lymphoma and leukemia</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Other neoplasms</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Accidents, poisonings, and violence‡</td>
<td>12 (26.7)</td>
</tr>
<tr>
<td>Other causes</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>45 (100.0)</strong></td>
</tr>
</tbody>
</table>

*International Classification of Diseases, Eighth Revision (ICD-8), codes 000-136.
†ICD-8 codes 140-239.
‡ICD-8 codes 800-900.
Another autopsy study of youth showed a relation of coronary atherosclerosis to an index of mean arterial pressure based on findings in small renal arteries. Correspondingly, a recent report on electron-beam computed tomography showed that, in young adults, BP related to presence of coronary artery calcification. It is reasonable to interpret our data as concordant, ie, indicating that such BP-related early atherosclerotic lesions lead to greater risk for fatal CVD during the decades from young adulthood through middle age.

Our data indicate that SBP may be more useful in predicting future CHD and CVD deaths than DBP. Risk generally increased throughout the range of SBP from 120 to 180 mm Hg and above. This finding for young adults lends support to recent assessments, based on data for older adults, that SBP might be more important than DBP and that both (SBP/DBP) merit consideration in assessment of CVD risk.

Although not statistically significant, our data on low DBP (<70 mm Hg) suggest it may be related to increased long-term CHD, CVD, and all-cause mortality and that low SBP (<120 mm Hg) may be related to increased all-cause mortality. These results should be interpreted with caution for several reasons. First, HRs were not significant and 95% CIs were wide, given small numbers of CHD and CVD deaths in these categories. Second, as footnoted in the BP classification of JNC-V and JNC-VI, people with very low BP, especially very low DBP, may have medical abnormalities, eg, aortic insufficiency or preclinical neoplastic disease, hence needing medical evaluation. We could not completely exclude men with medical conditions. After exclusion of those with low DBP (<60 mm Hg, also <65 mm Hg), risks for CHD and CVD mortality in the optimal and normal BP strata were almost identical. Therefore, it is reasonable to infer that these data do not critically bring into question the conclusion that the relationship between SBP/DBP and CVD risks is generally continuous (monotonic), and that for healthy adults, including young as well as older adults, SBP/DBP of less than 120/80 mm Hg (<120/<80 mm Hg) or of less than or equal to 120/80 mm Hg (<120/≤80 mm Hg) is optimal.

A limitation of the present study is that results were based on a single measurement of blood pressure, hence,
they probably underestimate true associations because of regression dilution bias. Nonetheless, as shown here and in many other prospective population studies, a single BP reading is strongly predictive of future CVD events. Since this cohort was identified at employment sites, the role of the “healthy worker effect” should be considered, ie, because working populations tend to be healthier than general populations, the mortality rate of the CHA cohort was about 30% lower than that expected for a similar sample of the general population. However, this phenomenon has little or no bearing qualitatively on the relation of baseline risk factors (including BP) to long-term mortality, as shown by many prospective studies with similar qualitative results on this matter for workplace-based and community-based populations samples. It is possible that because of this phenomenon, our study quantitatively underestimates absolute risk and absolute excess risks of adverse blood pressure levels for young adult men. Thus, it is a reasonable inference, supported by the limited data available from other studies of young adults, that these findings are generalizable.

Our results indicate that levels of blood pressure above normal in young adults is a large unsolved problem for medical care and public health. Long-term absolute risks and absolute excess risks, ie, from average age of 30 years at baseline to 55 years, were substantial for these young adult men, making up 61.9% of this cohort, with 59.4% of all excess deaths in men with high-normal BP and stage 1 hypertension.

These data lend strong support to 2 strategic concepts. First population-wide primary prevention by safe nutritional-hygienic means of adverse BP levels, highly prevalent at present in middle-aged and older people, is important. With such primary prevention, a substantial increase can be achieved in the proportion of people in the population who throughout life have favorable levels of BP (and other risk factors). Second, population-wide efforts should be made for early detection of children, teenagers, young adults, and others with unfavorable BP levels, so that therapeutic efforts can be instituted early, first and foremost, to improve lifestyles. Initial lifestyle recommendations to prevent and treat high BP involved avoidance of high levels of salt intake, inadequate potassium intake, excess alcohol use, overweight, and sedentary habit. Based on recent research advances, these recommendations have been expanded to include high intake of fruits, vegetables, whole grains, and legumes; fat-free and low-fat protein sources; and low intake of lipid-rich foods (ie, reduced dietary total fat, saturated fat, and cholesterol) and sweets.

Our results also support recommendations by JNC-VI on dealing with risks for persons aged 18 years and older with high BP. Because our study was observational, not interventional, it yielded no direct data related to treatment of high BP in young adults by lifestyle and (as indicated) pharmacological means. For hypertensive men of this age, there are no clinical trial data, no trials on-going, and to the best of our knowledge none planned, because sample size and duration are forbidding. Therefore, use of drugs for this age group must rely on judgment concerning the likely mix of benefit and risk with decades-long treatment. Our data are important evidence on risks; they reinforce JNC-VI recommendations to base drug (along with lifestyle) treatment on BP levels, findings for other risk factors and for target organ damage, and response to initial lifestyle intervention, and not on age.

In conclusion, the data of this study on young adult men underscore the soundness of recommendations for population-wide lifestyle modifications to prevent adverse BP levels, population-wide efforts for early detection and lifestyle counseling for those who already have unfavorable BP levels, and, for those with frank high BP at any adult age, implementation of JNC-VI guidelines for treatment.

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