Effect of Age on Blood Pressure Parameters and Risk of Cardiovascular Death in Men

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Background: Elevated blood pressure (BP) is a risk factor for cardiovascular disease (CVD), but it remains unclear which component—alone or in combination—is the best predictor. We sought to determine which BP parameters are important predictors of CVD death across a wide age range.

Methods: We used a prospective cohort study design with 53,163 men followed for cause-specific death during a median of 5.7 years in the Physicians’ Health Study enrollment cohort. Baseline age, systolic BP and diastolic BP were collected. We calculated relative risks (RRs) and their 95% confidence intervals using Cox proportional hazard models adjusting for major risk factors for CVD, and then stratified by age (39 to 49, 50 to 59, 60 to 69, and 70 to 84 years).

Results: There were 459 CVD deaths during follow-up. For each 10 mm Hg increase in systolic BP, the multivariable RRs by ascending age group were 1.46, 1.43, 1.24, and 1.13. The multivariable RRs for each 10 mm Hg increase in diastolic BP were 1.25, 1.20, 1.28, and 1.07. Compared with systolic BP, pulse pressure and mean arterial pressure were not consistent predictors across age ranges, and combining systolic BP with another parameter did not improve the model compared with using systolic BP alone in any age group (all \( P > .05 \)).

Conclusions: In this large cohort of healthy men with no history of hypertension, systolic BP was the most consistent and significant predictor of CVD death across all ages. Diastolic BP was not as strongly associated with risk. Our results support the continuing emphasis on using systolic BP in predicting cardiovascular risk. Am J Hypertens 2006;19:47–52 © 2006 American Journal of Hypertension, Ltd.

Key Words: Blood pressure, age groups, cardiovascular diseases, prospective studies.
Methods

Study Population

The Physicians’ Health Study (PHS) was a randomized, double-blind, placebo-controlled trial with a 2 by 2 factorial design testing whether 325 mg of aspirin taken every other day reduces CVD mortality and whether 50 mg of β-carotene taken every other day decreases the incidence of cancer. The PHS was approved by the Brigham and Women’s Hospital Institutional Review Board. In 1982 and 1983, letters were sent to 261,248 US male physicians on the American Medical Association mailing list that included an invitation to participate in the trial, informed consent forms, and a questionnaire to provide baseline information. By the end of 1983, 112,528 physicians had responded to the mailing and returned an initial enrollment questionnaire. Our study evaluated the 53,163 respondents aged 39 to 85 years who provided self-reported BP, had no past or current treatment for hypertension, and had no history of myocardial infarction (MI), stroke, cancer, transient ischemic attack (TIA), gout, peptic ulcer, or liver disease.

Ascertainment of BP Measures and Covariates

On the baseline questionnaire, participants reported CVD risk factors including age, height (inches), weight (pounds), prior or current treatment for hypertension or hypercholesterolemia (yes/no), cigarette smoking (never, past, <20 cigarettes/d, or ≥20 cigarettes/d), frequency of exercise (<1/week or ≥1/week), alcohol use (rarely/never, <1 per week, ≥1 per week), history of diabetes mellitus (yes/no), current use of aspirin (≥1/week), and current use of multivitamins (≥1/week). Body mass index (in kilograms per meters squared) was calculated using weight and height. Self-reported systolic BP and diastolic BP were collected, which have been highly correlated with measured systolic BP (r = 0.72) and diastolic BP (r = .60) in a sample of physicians. We then calculated PP (defined as systolic BP – diastolic BP) and MAP (defined as 1/3 systolic BP + 2/3 diastolic BP).

Ascertainment of CVD Mortality

Cardiovascular disease death was the end point for this study. Using the National Death Index in 1990, death certificates were obtained for the respondents who died before the end of 1989. The deaths were classified by trained nosologists using the first revision of the Ninth International Classification of Diseases in conjunction with the Automated Classification of Medical Entities Decision Tables to manually select underlying cause of death. This analysis included total CVD mortality (ICD codes 390 to 459), which consisted of ischemic heart disease, MI, cerebrovascular disease, and other CVD.

Statistical Analysis

Analyses were stratified a priori by age at baseline as 39 to 49, 50 to 59, 60 to 69, and 70 to 84 years. Means or proportions of baseline variables were computed for each group. We examined the BP distributions in each group, along with stratum-specific Spearman correlation coefficients for the four measures of BP. Cox proportional hazard models were used to examine the association of individual and combined BP parameters and the risk of CVD death. For each age group, BP parameters were added to the multivariable model as follows: systolic BP; diastolic BP; systolic BP and diastolic BP; PP; systolic BP and PP; MAP; systolic BP and MAP. This strategy was based on a prior analysis limited to randomized PHS participants.

We conducted both age and multivariable-adjusted analyses that added BMI, history of diabetes, alcohol use, cigarette smoking, exercise, aspirin and multivitamin use. We did not adjust for history of hyperlipidemia because >10% of data were missing from participants. Adjusting for major cardiovascular risk factors introduced 11 degrees of freedom (df). We considered the relative risks (RRs) of CVD death for 10 mm Hg increases in BP parameters.

We compared the prognostic significance of each model by performing likelihood ratio (χ²) tests for the difference in likelihood ratios between two models. All RRs were presented with 95% confidence intervals (CIs), and all reported P values were two-sided. Analyses were performed using SAS version 8.2 (Cary, NC).

Results

Overall, the mean age of participants in this study was 53.0 ± 9.7 years, whereas the mean systolic BP was 124.8 ± 11.1 mm Hg, mean diastolic BP was 78.0 ± 7.0 mm Hg, mean PP was 46.9 ± 8.8 mm Hg, and mean MAP was 93.6 ± 7.6 mm Hg. Table 1 compares the four BP parameters and other characteristics divided into four age groups (39 to 49, 50 to 59, 60 to 69, and 70 to 84 years). As expected, the average systolic BP, PP, and MAP increased continuously from the youngest to the oldest age group, whereas levels of diastolic BP remained similar across all ages. Body mass index was similar by age, whereas the prevalence of diabetes steadily increased from younger to older men. Older participants were less likely to be current smokers or report a history of hyperlipidemia. Aspirin and multivitamin use were both higher in the older age groups, whereas vigorous exercise was slightly lower.

Spearman correlations between systolic and diastolic BP by ascending age group were 0.63, 0.63, 0.61, and 0.50 (all P values < .001), demonstrating a high correlation that diminished slightly in the oldest age group. The MAP was highly correlated with systolic and diastolic BP in all age groups, with Spearman correlations ranging from 0.85 to 0.92 (all P values < .001), whereas MAP was more
modestly correlated with PP, ranging from 0.27 to 0.48 (all \( P \) values < .001). The PP and diastolic BP had Spearman correlations ranging from −0.07 to 0.06, but all other comparisons of BP components were highly correlated.

During a median follow-up of 5.7 years, there were 459 confirmed cases of CVD death. During the course of the study, 0.2% of men aged 39 to 49 years died from CVD as compared with 4.8% of men aged 70 to 84 years.

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The multivariable RRs (95% CI) for each 10 mm Hg increase in a BP parameter were assessed for the entire cohort (Table 2). Each of the individual BP components was significantly associated with an increased risk of CVD death (all \( P < .05 \)). Because systolic BP was the most consistent predictor of CVD death, we considered whether adding another BP parameter would enhance a multivariable model containing systolic BP alone. When we added diastolic BP to the model, systolic BP remained a significant predictor (RR = 1.26; 95% CI, 1.15–1.38), while diastolic BP was no longer predictive (RR = 0.95; 95% CI, 0.82–1.12). Accordingly, the combined model did not improve the fit compared to using systolic BP alone (Δ-2 Log L = 0.346). Similarly, the addition of PP or MAP to the model with systolic BP alone did not improve prognostic significance.

For each of the four BP parameters, we calculated the multivariable RRs across the age groups and these results are presented in Fig. 1. All of the BP parameters were predictors of CVD death with attenuated RRs in the older age ranges. From youngest to oldest age, systolic BP had a multivariable RR of 1.46 (95% CI, 1.08–1.98), 1.43 (95% CI, 1.21–1.69), 1.24 (95% CI, 1.09–1.41), and 1.13 (95% CI, 0.99–1.27). The corresponding RRs for diastolic BP were 1.25 (95% CI, 0.76–2.08), 1.20 (95% CI, 0.90–1.61), 1.28 (95% CI, 1.00–1.64), and 1.07 (95% CI, 0.86–1.34). The multivariable RRs for PP and MAP also decreased across the four age ranges.

Because systolic BP was a consistent predictor of CVD death in the analysis of the entire cohort and systolic BP is the easiest to use clinically, we considered whether adding another BP parameter would enhance the predictive ability of any model across ages (Table 3). Consideration of an additional BP parameter did not improve a multivariable model that already contained systolic BP (all \( P < .05 \)). The corresponding RRs for diastolic BP were 1.25 (95% CI, 0.76–2.08), 1.20 (95% CI, 0.90–1.61), 1.28 (95% CI, 1.00–1.64), and 1.07 (95% CI, 0.86–1.34). The multivariable RRs for PP and MAP also decreased across the four age ranges.

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**Discussion**

In this prospective cohort study of 53,163 apparently healthy men without diagnosed hypertension, we found that systolic BP alone was a strong, consistent, and independent predictor of CVD death for men aged 39 to 84 years old. Using systolic BP with another BP parameter did not improve the prognostic significance in any age range. Diastolic BP alone was a weaker predictor and did not add prognostic information to models already containing systolic BP. Pulse pressure and MAP were also inde-
We previously reported in 11,150 randomized physicians that systolic BP, diastolic BP, and MAP were associated with incident CVD (including MI, angina pectoris, coronary artery bypass graft surgery, percutaneous transluminal coronary angioplasty, stroke, and CVD death) in those aged <60 years, whereas either systolic BP or PP may be used for those aged ≥60 years. The present study assessed only CVD mortality among a larger group of 53,163 physicians who met our inclusion and exclusion criteria and had subsequent mortality status determined using the National Death Index. Among men aged 39 to 49 years in the present study, both systolic BP and PP were significantly associated with an increased risk of CVD death, although the number of events in this group was lowest. Among men aged 50 to 59 years and 60 to 69 years, systolic BP, PP, and MAP were all significant predictors of CVD death. Among the oldest men in our cohort (70 to 84 years), the RRs for all the BP parameters were attenuated but each risk estimate remained elevated.

Our results are consistent with those found for incident CVD in the smaller cohort of randomized physicians. Our results compare favorably with previously published studies evaluating BP parameters. Systolic BP, PP, and MAP all increased continuously across age ranges, whereas diastolic BP remained constant; an observation consistent with other population-based cohorts. In addition, the Cardiovascular Health Study found systolic BP to be the best predictor of CVD death in a cohort of older subjects, many of whom had hypertension. In a population-based study with subjects not taking antihypertensive medications, systolic BP was the clinically superior measure of risk for CVD and in a European study, systolic BP was a stronger predictor than diastolic BP. Among those with measured normal BPs and aged 45 to 57 years in the MRFIT study enrollment cohort, systolic BP was superior to diastolic BP and PP for predicting CVD risk. Although combining systolic BP with diastolic BP did add predictive value among MRFIT participants with hypertension, our results among men with lower BPs did not independently associated with CVD death, but neither improved on models already containing systolic BP.

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support the use of combination models. Among participants aged 50 to 79 years in the Framingham Heart Study, neither systolic nor diastolic BP was superior to PP in predicting CVD risk.\(^{25}\) Further analysis demonstrated an age effect on CVD risk that leads to a shift in importance from diastolic BP (<50 years) to systolic BP (50 to 59 years) and then to PP (≥60 years).\(^{6}\) In our study, systolic BP was a consistent predictor of CVD death across a similar age range.

Elevated BP is linked to an increased risk of CVD through a variety of pathophysiologic mechanisms. Arterial stiffness, which may be due to atherogenesis, may lead to the development of higher BPs.\(^{24}\) Higher systolic BP levels reflect the stiffening of the arterial walls in areas exposed to increased pressure.\(^{25}\) Diastolic BP may be related to coronary perfusion of the myocardium. Higher PP levels can be the result of arterial stiffening that leads to increased systemic load and subsequent risk of CVD death.\(^{26,27}\)

Our study has several limitations. Systolic and diastolic BP were self-reported, but among physician groups self-reported BP is highly correlated with measured values.\(^{18}\) Although our CVD death rate was low, we had a large study cohort and used a centralized computerized index to obtain death records and achieve follow-up for cause-specific end points. Although we excluded men with any diagnosis or treatment for hypertension at baseline, some participants may have subsequently taken antihypertensive medications to lower their BP, and this may lead to an underestimation of the risk associated with BP and CVD death. Our participants were healthy male physicians and this may affect the generalizability to other populations; however, we have no reason to believe that the biological mechanism by which BP may be associated with CVD death is unique to our study population.\(^{28,29}\) Finally, we adjusted for major confounders in our multivariable models, but as in any observational study residual confounding may have affected our results.

In conclusion, systolic BP alone was a strong and consistent predictor of CVD death in men across a wide age range. Although diastolic BP, PP, and MAP were also associated with elevated risk, none of these other BP parameters was superior in determining risk or enhanced multivariable models that already contained systolic BP. Using systolic BP alone was sufficient to determine the risk of CVD death, and these results are consistent with the continuing emphasis on the clinical use of systolic BP to predict the risk of incident cardiovascular disease.\(^{5,30}\)

### Table 3. Comparison of Cox multivariable* RR (95% CIs) of cardiovascular death for SBP and three other blood pressure parameters among men in four age ranges

<table>
<thead>
<tr>
<th>Age Range</th>
<th>SBP†</th>
<th>DBP†</th>
<th>SBP†</th>
<th>PP†</th>
<th>MAP†</th>
</tr>
</thead>
<tbody>
<tr>
<td>39–49 y</td>
<td>1.52 (1.08–2.15)</td>
<td>0.86 (0.49–1.57)</td>
<td>1.34 (0.81–2.21)</td>
<td>1.14 (0.64–2.05)</td>
<td>1.63 (0.94–2.84)</td>
</tr>
<tr>
<td>50–59 y</td>
<td>1.56 (1.28–1.89)</td>
<td>0.78 (0.56–1.10)</td>
<td>1.21 (0.92–1.61)</td>
<td>1.28 (0.91–1.80)</td>
<td>1.76 (1.27–2.44)</td>
</tr>
<tr>
<td>60–69 y</td>
<td>1.23 (1.05–1.43)</td>
<td>1.03 (0.77–1.38)</td>
<td>1.27 (0.99–1.62)</td>
<td>0.97 (0.72–1.30)</td>
<td>1.21 (0.92–1.58)</td>
</tr>
<tr>
<td>79–84 y</td>
<td>1.14 (0.99–1.31)</td>
<td>0.96 (0.75–1.24)</td>
<td>1.09 (0.87–1.36)</td>
<td>1.04 (0.81–1.34)</td>
<td>1.16 (0.92–1.46)</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

* Adjusted for age, tobacco use, body mass index, diabetes, alcohol intake, exercise, aspirin use, and multivitamin use.
† per 10 mm Hg.

### References


