Blood Pressure Parameters and Risk of Fatal Stroke, NHANES II Mortality Study

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Background: Recent studies have suggested that systolic blood pressure (BP) is a better predictor of stroke than diastolic BP in apparently healthy white men. Whether these relationships are similar for women and African Americans remains unclear.

Methods: We used data from 6667 (3205 men; 3462 women) adults from the Second National Health and Nutrition Examination Survey Mortality Study to examine whether the relative risk of fatal stroke was associated with a 10 mm Hg increase in BP parameters (systolic BP, diastolic BP, pulse pressure, and mean arterial pressure).

Results: During a median of nearly 15 years of follow-up, 113 fatal strokes (62 men; 51 women) occurred. Systolic BP was associated with an increased risk of fatal stroke for men (relative risk [RR] = 1.19), women (RR = 1.15), whites (RR = 1.17), and African Americans (RR = 1.28) after multivariable adjustment (all, $P \leq .05$). Results for other BP parameters were not consistent; simultaneous consideration of two parameters did not improve prediction of fatal stroke over systolic BP alone.

Conclusions: Our results agree with previous studies that indicate systolic BP is an important predictor of stroke risk for all groups within the population and provide further evidence of the need to control systolic BP in the population. Am J Hypertens 2007;20:338–341

Key Words: Systolic blood pressure, diastolic blood pressure, stroke.

Hypertension, an important risk factor for stroke, affects nearly 65 million Americans.[1] Efforts to treat and control elevated blood pressure (BP) initially relied heavily on diastolic BP.[2] Results from the Systolic Hypertension in the Elderly Program (SHEP) trials performed in the late 1980s and early 1990s, however, shifted the focus to systolic BP.[3] Recently, increased attention has been given to pulse pressure (PP) (defined as systolic BP − diastolic BP) and mean arterial pressure (MAP) (defined as ⅔ diastolic BP + ⅓ systolic BP) as a predictor of cardiovascular disease (CVD) and stroke.[4–7] Bowman and colleagues recently reported that of the four BP parameters (systolic BP, diastolic BP, PP, MAP), systolic BP was a consistent and more significant predictor of CVD[6] and stroke[7] death among a sample of healthy, predominantly white men from the Physician's Health Study. Whether these results are similar for men and women, and for African Americans and whites, remains unknown.

We used data from the Second National Health and Nutrition Examination Survey (NHANES II) Mortality Study, a nationally representative cohort of US adults, to examine the risk of fatal stroke associated with systolic BP, diastolic BP, PP, and MAP stratified by gender and ethnicity. Similar to Bowman and colleagues,[6,7] we considered the BP parameters individually and systolic BP in combination with the other three parameters to examine whether two BP parameters improved the prediction of stroke events.

Methods

The Centers for Disease Control and Prevention conducted NHANES II between 1976 and 1980. NHANES II, a nationwide probability sample of approximately 28,000 children and adults, was designed to be representative of the civilian, noninstitutionalized US population. A detailed description of the NHANES II survey and sampling procedures is available elsewhere.[8]

As part of NHANES II, persons underwent a physical examination by a physician. At the beginning of the examination the physician measured the sample person's BP (in mm Hg) while the individual was in a sitting position. Blood pressure was taken twice more at the end of the examination, once while the person was recumbent and again while sitting. Thus, three BP readings were measured according to American Heart Association guidelines[9] at baseline. The BP measurement used in this

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analysis was the mean value of the second and third readings. Serum cholesterol concentrations (in milligrams per deciliter), height (in centimeters), and weight (kilograms) were measured. Participants also completed a medical history that included questions about CVD, physical activity, and cigarette smoking, including a lifetime smoking history and current smoking status (yes/no). Former smokers were those who had smoked ≥100 cigarettes during their lifetime but who were not currently smoking.

We merged baseline data from NHANES II with follow-up data from the NHANES II Mortality Study, a prospective cohort study of 9252 adults aged 30 to 75 years at the time of their NHANES II examination.[10] As part of the Mortality Study, data from the National Death Index, which has been shown to capture 93% to 98% of all US deaths,[11–13] and from the Social Security Administration Death Master File were used to ascertain the vital status of each cohort member through December 31, 1992 (approximately 17 years of follow-up). Information obtained from the Mortality Study data included the month and year in which a person was last known alive and the International Classification of Diseases, 9th revision (ICD-9) code for the cause of death. We used the 15th day of the month in our analysis as the day of the date last known alive for decedents. For all others, December 31, 1992, was considered the last known date alive. Survival time was calculated as the difference between the NHANES II baseline examination date for each person and the last known date alive obtained from the Mortality Study. Multiple causes of death were available for 98% of decedents.

From the Mortality Study cohort (n = 9252), we excluded those lost to follow-up, with missing data for study variables, as well as those who were not either white or African Americans, who reported a history of stroke or coronary heart disease, or who were currently using antihypertensive medications. A total of 6667 (3205 men; 3462 women) participants with complete information were included in the analysis.

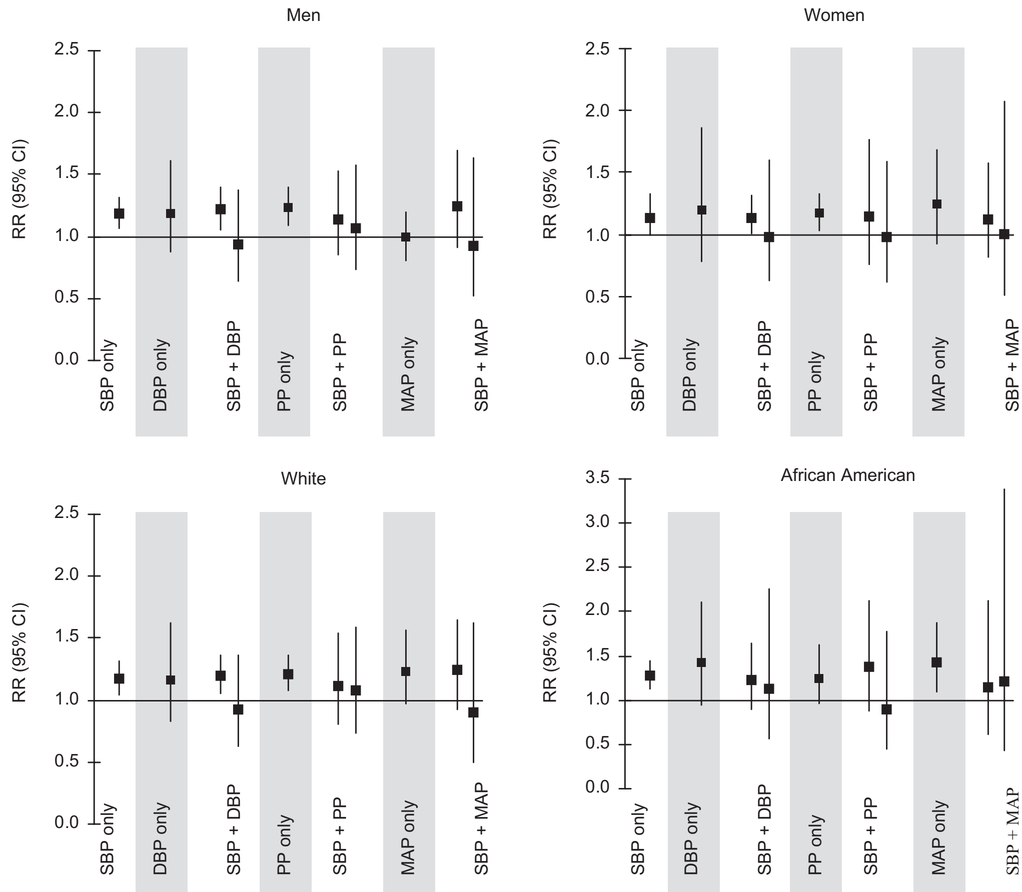
The outcome for the study was fatal stroke defined by ICD-9 codes 430–438, excluding code 435 (eg, transient ischemic attack). We used Cox proportional hazards regression to estimate, by means of the hazard ratio, the relative risk (RR) of fatal stroke associated with a 10 mm Hg increase in each of the four BP parameters in regression models adjusted for age (continuous), gender, ethnicity (white, African American), education (<12 years, 12 years, >12 years), physical activity (moderate or inactive, moderate, more than moderate), body mass index (defined as weight in kg/height in meters squared; continuous), smoking status (current, former, never), aspirin use, total serum cholesterol (continuous), and diabetes (yes, no). Each BP parameter was first modeled individually. We then examined models with two BP parameters. We used likelihood ratio tests ($LR = -2 \ln L_1 - [-2 \ln L_2]$) to compare regression models. We also assessed collinearity between BP parameters using Pearson correlation coefficients and multicollinearity diagnostic statistics (tolerance and variance inflation factors [VIF]). Although there is no formal cutoff value to use with the VIF for determining the presence of multicollinearity, values of VIF exceeding 10 are often regarded as indicative of multicollinearity. The VIF values >2.5 may be cause for concern. To remain consistent with the work of Bowman and colleagues in a nationally representative cohort, we followed their manner of analyses while reporting VIF values.

To make the NHANES representative of the US population, sample weights were used in all analyses. Statistical analyses were completed using SAS v8.0 (SAS Institute, Cary, NC) and SUDAAN (Research Triangle Institute, Research Triangle Park, NC). Models were fit to the data using SUDAAN to account for the complex sampling design and to achieve accurate variance estimates. Categorical variables were compared between groups with a χ^2 test; continuous variables were compared between groups with ANOVA. We assessed the appropriateness of the proportional hazard assumption for the variables in our final model with log–log survival plots and Schoenfeld residual plots. Without exception, all covariates in the final model satisfied the proportional hazard assumption. Model parameter estimates were computed by maximum likelihood techniques. Relative hazards were obtained by exponentiating estimated regression model coefficients, and 95% confidence intervals (CIs) were based on the standard error of the model coefficients. All statistical inferences were based on a significance level of .05.

Results

A total of 6667 (3205 men; 3462 women) adults were included in the analysis. The mean age (standard error of mean) of the sample was 47 (0.25) years. The average systolic BP/diastolic BP was 127/79 mm Hg (124/77 mm Hg for women; 130/82 mm Hg for men). Pearson correlation coefficients were 0.717 for systolic BP versus diastolic BP, 0.815 for systolic BP versus PP, 0.913 for systolic BP versus MAP, 0.181 for diastolic BP versus MAP, 0.939 for diastolic BP versus MAP, and 0.509 for PP versus MAP (all, $P < .001$) (data not shown). The VIF for systolic BP was 2.5 and diastolic BP VIF was 2.3 within the systolic BP–diastolic BP parameter pair. Systolic BP VIF was 3.9 and PP VIF 3.7 within the systolic BP–PP parameter pair, and systolic BP VIF was 7.2 and MAP VIF was 6.9 within the systolic BP–MAP parameter pair.

During follow-up (median = 14.6 years), there were 113 fatal strokes (62 men; 51 women). Persons who died from stroke were older (48% v 10% ≥65 years, $P < .001$), and more likely to be men (59% v 48%, $P = .019$), less educated (26% v 16% <12 years, $P = .006$), physically inactive (18% v 13%, $P = .034$), and have diabetes (10% v 3%, $P = .027$). Overall, mean systolic BP ($P < .001$), diastolic BP ($P = .051$), PP ($P < .001$), and MAP ($P < .001$) values were greater for those who died from stroke compared to those who did not, although these patterns differed somewhat by age. For example, BP parameters



* Adjusted for age, sex, race/ethnicity, education, smoking, physical activity, diabetes, body mass index, aspirin use, and total cholesterol concentration.

FIG. 1. Multivariable-adjusted relative risk (RR) for fatal stroke associated with a 10 mm Hg increment in blood pressure parameters by gender and ethnicity. Adjusted for age, sex, race/ethnicity, education, smoking, physical activity, diabetes, body mass index, aspirin use, and total cholesterol concentration. SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure; MAP = mean arterial pressure.

were similar or slightly lower for fatal stroke cases than for those who did not die among adults 65 to 74 years.

After multivariable adjustment, each of the individual BP parameters was associated with an increased risk of fatal stroke for the total sample (systolic BP: 1.18 [95% CI, 1.07–1.31]; diastolic BP: 1.21 [95% CI, 0.92–1.59]; PP: 1.22 [95% CI, 1.10–1.35]; MAP: 1.26 [95% CI, 1.03–1.54]). Estimates for diastolic BP did not attain statistical significance in stratified analyses for men or women (Fig. 1). In addition, MAP estimates were not statistically significant for men, women, or whites. The addition of a second BP parameter to a model containing systolic BP did not improve model fit (*P* value for LR test $> .05$, all). Addition of a diastolic BP, PP, or MAP parameter to the systolic BP model resulted in a positive association between systolic BP and the risk of fatal stroke, whereas the associations for the second parameter were attenuated and no longer predictive; statistically significant RRs ($P < .05$) were observed for systolic BP RR, 1.20 [95% CI, 1.07–1.33] only in conjunction with diastolic BP. Similar results were observed after stratifying on ethnicity (white versus African Americans) (Fig. 1).

Discussion

The prevalence of hypertension, which affects nearly one in three US adults, increased nearly 30% (from 50 to 65 million adults) in the US between 1988–1994 and 1999–2000.[1] The lifetime risk of developing hypertension among middle-aged and older adults is 90%.[14] In this study of a nationally representative cohort of men and women, systolic BP was independently associated with an increased risk of fatal stroke among men and women and among whites and African Americans. Other BP parameters did not consistently predict fatal stroke. Inclusion of two BP parameters did not improve model fit versus models with systolic BP alone.

Our findings complement those from similar studies of BP parameters and risk of stroke. Bowman and colleagues[7] observed significant associations between all four

BP parameters and stroke mortality among 11,467 apparently healthy men from the Physician's Health Study after a median of approximately 19 years of follow-up (508 stroke deaths). Only systolic BP was consistently associated with stroke death and models with two BP parameters did not fit the data better than models with systolic BP alone. Similar findings were observed for CVD deaths among 53,163 apparently healthy men from the Physician's Health Study after a median of nearly 6 years of follow-up (459 CVD deaths).[6] In the 1963 Israeli Ischemic Heart Disease study that followed 9611 male civil servants aged 40 to 65 years for approximately 23 years, Weitzman and Goldbourt[5] also observed significant associations between all four BP parameters and fatal stroke (339 stroke deaths). Results for models with two BP parameters differed across normotensive, hypertensive, and isolated systolic hypertensive strata. For example, systolic BP but not diastolic BP was a significant predictor of stroke death among normotensive men, whereas both systolic and diastolic BP were significant predictors among hypertensive men and men with isolated systolic hypertension. In other two BP parameter models, PP and diastolic BP were significant predictors of fatal stroke among normotensive and hypertensive men, whereas PP and MAP were both significant predictors of fatal stroke among normotensives but not hypertensives.

There are several possible explanations for differences between studies. We used the average of multiple BP measurements obtained by physicians in a standardized environment, whereas BP measurements from the Physician's Health Study were self-reported. We had limited power to detect a significant effect of BP on risk of fatal stroke due to a small number of stroke events and we were unable to stratify on stroke type. It is possible that relationships between BP parameters and stroke differ by the type of event (eg, ischemic versus hemorrhagic), although Bowman and colleagues[7] reported similar relationships for total (RR: 1.30; 95% CI: 1.20–1.42), ischemic (1.27; 1.16–1.40), and hemorrhagic (1.38; 1.13–1.68) stroke. Our study included men and women, whereas the other studies focused only on men. We included African-Americans in this analysis; the Physician's Health Study cohort was predominantly white.[14] Finally, collinearity diagnostics indicated possible issues with certain BP parameter combinations.

In conclusion, results from the NHANES II Mortality Study agree with those from previous studies and show that systolic BP is an important risk predictor for fatal stroke. These relationships were observed among men and women, as well as among whites and African Americans and provide further evidence of the need to control systolic BP in the population.

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