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Original Study

Observed Blood Pressure and Mortality Among People Aged 65 Years and Older: A Community-Based Cohort Study

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A B S T R A C T

Objectives: The 2014 Eighth Joint National Committee guidelines for hypertension management emphasize the upper limit of blood pressure (BP) as the target for treatment in the elderly population. Given the uncertainty regarding optimal BP range, we aimed to investigate the association between observed BP and subsequent mortality in older people.
Design, setting, and participants: We extracted data from 128,765 participants ≥65 years of age who underwent annual health examinations in a retrospective, observational community-based study from 2001 to 2010. Seated BP was measured using an oscillometric device. The outcomes were all-cause and cardiovascular mortality.
Results: As compared to participants with systolic BP at 130 to 139 mm Hg, the risk of all-cause mortality was significantly higher among those with <110 (adjusted hazard ratios [aHRs], 1.12; 95% confidence interval [CI], 1.05-1.20), 140 to 149 (aHR, 1.08; 95% CI, 1.03-1.14), 150 to 159 (aHR, 1.07; 95% CI, 1.01-1.17), 160 to 169 (aHR, 1.11; 95% CI, 1.04-1.19), and ≥170 mm Hg (aHR, 1.25; 95% CI, 1.17-1.33), whereas the differences were not significant for those with 110 to119 (aHR, 1.06; 95% CI, 1.00-1.12) and 120 to 129 mm Hg (aHR, 1.03; 95% CI, 0.97-1.08). Similarly, diastolic BP at 40 to 79 mm Hg was associated with the lowest risk of all-cause mortality. The J-shaped curve relationship between BP and cardiovascular mortality was also observed.
Conclusions: Observed systolic and diastolic BP other than 110 to 139 and 40 to 79 mm Hg, respectively, were associated with a worse outcome. Our large cohort study supports the J-shaped mortality with observed BP in older people.

The 2014 Eighth Joint National Committee (JNC 8) panel recommendations for the management of high blood pressure (BP) raised the systolic BP (SBP) goal for the treatment of antihypertensive therapy from 140 to 150 mm Hg in the general population aged ≥ 60 years,[1] because available randomized, controlled trials (RCTs)[2–4] only conferred a significant reduction of cardiovascular risk in the treatment of those with SBP ≥ 150 mm Hg. Given the limited trials of examining SBP targets lower than 150 mm Hg in older

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populations, there has been substantial debate regarding increasing the BP target in this population without strong evidence. In addition, data from the National Health and Nutrition Examination Surveys (NHANES) for 2005 to 2010 demonstrated that hypertension control to less than 140/90 mm Hg remained for over half of the older adults in the US.[5] For these individuals, however, their BP management was only on the basis of expert opinion, as the panel suggested no need to adjust their medication to increase their BP if they followed the JNC 7 recommendation to achieve an SBP ≤ 140 mm Hg without additional adverse effects.[1]

Two Japanese RCTs of older people[6,7] evaluating SBP targets lower than 140 mm Hg failed to demonstrate additional benefits of cardiovascular events during a mean follow-up of 2 to 3 years, but both trials were underpowered. A subgroup analysis (age > 63 years) of an Italian open-label RCT[8] for patients' SBP intended to treat those with <130 mm Hg (tight control) compared with those with <140 mm Hg (usual control) showed inconsistent results in which tight BP control was beneficial for those aged > 70 but insignificant for those aged 63 to 70.

Because the U- or J-shaped association between BP and mortality has been shown in persons with newly diagnosed diabetes,[9] coronary artery disease,[10] and end-stage renal disease,[11] the association of BP and mortality in older populations remains controversial, with many observational studies showing the absence of such a relationship[12,13] or even a linear[14–16] or U-shaped relationship.[17–20] Most of these studies, however, were limited by small sample sizes, short follow-up periods, or mixed populations. Although the recent Systolic Blood Pressure Intervention Trial (SPRINT)[21] reported the benefits of blood pressure lowering to 120 mm Hg in a small elderly patient subgroup (≥75 years), the optimal BP level in older populations remains undetermined. Large-scale observational data may be useful to better understand the optimal BP target for older populations in real-world settings. We, therefore, conducted a large-scale community-based study to clarify this association for individuals older than 65 years of age by using the Taipei City Elderly Health Examination Database.

Methods

Study Design and Population

This retrospective community-based cohort study was performed based on data from the Taipei City Elderly Health Examination Database that was designed to improve older citizens' health and well-being by providing free annual health check-ups for citizens ≥65 years of age starting in 2001. This endeavor was completely sponsored by the Taipei City Government. Older citizens were encouraged to participate in this program on a voluntary basis, and they gave written informed consent for using their medical records exclusively for research purposes. They received health examinations in medical facilities contracted with the Taipei City Government following the identical standardized protocol. Details on the health examinations and data in the database have been described previously.[22,23] This database is linked to Taiwan's National Death Registry through the use of the participants' original identification numbers. To protect privacy, the data were eventually encrypted to generate de-identified secondary data maintained by the Department of Health of the Taipei City Government. The institutional review board of the Taipei City Hospital approved the present study (TCHIRB-1010323-E, TCHIRB-1030601-W).

Data Collection

From the Taipei City Elderly Health Examination Database, data of participants who had their BP measured at least once between 2001 and 2010 were extracted. We excluded individuals with a history of end-stage renal disease. At each clinic visit, individuals' seated brachial BP and pulse were measured using a calibrated oscillometric device following a standardized protocol.[24] The participants' past medical history, including any drugs they were taking, was obtained using a self-reported questionnaire. Their body weight, height, and smoking and alcohol habits were also recorded. A blood specimen after overnight fasting was collected for biochemistry analysis (including complete blood cell count), blood urea nitrogen, serum creatinine, albumin, uric acid, fasting glucose levels, and lipid profiles. Missing data were replaced by mean imputations of the entire cohort.

Outcomes

Mortality data were obtained from the national death registry system and coded from death certificates according to the International Classification of Diseases (ICD-9 or ICD-10). The primary outcome was all-cause mortality (ICD-9 001.x–999.x or ICD-10 A00.x–Z99.x). The secondary outcome was cardiovascular-related death (ICD-9 390.x–459.x; ICD-10 I05.x–I99.x). All participants were followed until death or December 31, 2010.

Statistical Analysis

The baseline BP values were used in the analyses. The BP values were categorized into SBP increments of 10 mm Hg (<110, 110-119, 120-129, 130-139, 140-149, 150-159, 160-169, and ≥170 mm Hg). Similar analyses were performed using diastolic BP (DBP) increments of 10 mm Hg in the following manner: < 40, 40-49, 50-59, 60-69, 70-79, 80-89, 90-99, and ≥100 mm Hg. Differences in the distributions of continuous and ordinal variables were tested using the Kruskal-Wallis test and for categorical variables, the chi-square test. We used the cubic splines (knots at intervals of 20 mm Hg between 110 and 170 mm Hg for SBP and between 40 and 100 mm Hg for DBP) in the Cox proportional hazard models to determine the nadir where the risk was lowest. In this model, 130 mm Hg for SBP and 70 mm Hg for DBP were chosen as the reference. Reference ranges do not influence the shape of the spline across the full range of exposure. These analyses were also performed in subgroups on the basis of age, gender, use of antihypertensive medication, established cardiovascular disease, diabetes mellitus, and chronic kidney disease (CKD) (defined as baseline estimated glomerular filtration rate <60 mL/min). The cumulative incidences of all-cause and cardiovascular mortality in cohorts were calculated using the Kaplan-Meier method, and they were compared with the log-rank test. Cox proportional hazard models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) among different SBP and DBP categories for all-cause and cardiovascular mortality. The reference category for SBP and DBP included the nadir value of the cubic spline curve of SBP and DBP, respectively. Adjusted HR was calculated by adjusting for age, gender, body mass index, smoking status, alcohol use, SBP or DBP, pulse rate, estimated glomerular filtration rate (calculated using the Chronic Kidney Disease Epidemiology Collaboration equation), diabetes mellitus, coronary artery disease, cerebrovascular disease, serum total cholesterol, triglycerides, high-density lipoprotein cholesterol, hemoglobin, fasting glucose, albumin, and uric acid. All statistical analyses were conducted using STATA statistical software (version 13.0; StataCorp, College Station, Texas). Statistical significance was defined as $P < .05$.

Results

Clinical Characteristics of the Study Population

At study entry, a total of 128,765 older people who met the inclusion criteria were identified (Appendix Figure 1). The baseline characteristics of the study population are shown in Table 1 and