Prognosis of Prehypertension Without Progression to Hypertension

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Even mild blood pressure (BP) elevations manifesting as prehypertension have been associated with cardiovascular disease (CVD) risk.[1,2] However, this risk could be attributable to the fact that many individuals with prehypertension eventually progress to overt hypertension.[2,3] The prognosis of prehypertension among individuals who never progress to hypertension and, in turn, the role of early versus late-onset prehypertension in this context remains unclear. Therefore, we conducted an investigation in the Framingham Heart Study to assess the long-term risks related to early- and late-onset prehypertension without progression to hypertension.

We used data collected from serial examinations attended by the Framingham Original (28 examinations in 1948–2005 at 2-year intervals) and Offspring (9 examinations in 1971–2014 with 4- to 8-year intervals) cohorts.[4] Of all 10 333 participants, we excluded individuals who had unknown hypertension status onset age (ie, ≥55 years of age with prehypertension or hypertension present at baseline, n=788), did not attend any follow-up examinations (n=451), could not reach 60 years of age by the second-to-last examination (n=974), had not died before December 31, 2014 (n=2283; mean baseline 36.2±6.5 years of age, 57.7% women), or had missing covariates when hypertension status was ascertained (n=244). The final sample for analyses included n=5593. Three physicians adjudicated causes of death as previously described.[4] Boston University Medical Center's institutional review board approved the study protocols, and each participant provided written informed consent.

We defined prehypertension as BP 120 to 139/80 to 89 mm Hg and hypertension as BP ≥140/90 mm Hg or use of antihypertensive medication,[5] with both categories assessed at ≥2 consecutive examinations. We categorized participants into 5 phenotypes: (1) never prehypertension or hypertension (n=342), (2) late-onset prehypertension without ever developing hypertension (n=354), (3) early-onset prehypertension without ever developing hypertension (n=926), (4) late-onset hypertension (*n*=1632), and (5) early-onset hypertension (n=2339). We defined early onset as <55 years of age on the date of first examination at which criteria for hypertension were met. Because the dates of prehypertension/hypertension onset were not available at baseline and ≈2/3 of the participants had died by the last follow-up date, we investigated the relation among the 5 BP phenotypes and cause-specific mortality using a case-control design. Cases were considered persons who died from CVD (n=1757; death from coronary heart disease [CHD], stroke, heart failure, or other vascular event) or specifically from CHD (n=951), and controls included the remaining 3836 decedents. We used logistic regression to estimate case-versus-control odds ratios for the 4 prehypertension/hypertension categories versus those who died without ever developing prehypertension or hypertension. All models adjusted for age at death, sex, smoking, total cholesterol, cohort, and diabetes mellitus. Data on smoking, cholesterol, and diabetes mellitus were obtained from the last examination cycle at which data were available. We fit LOESS-smoothed curves for mean systolic BP values (+10 mm Hg for

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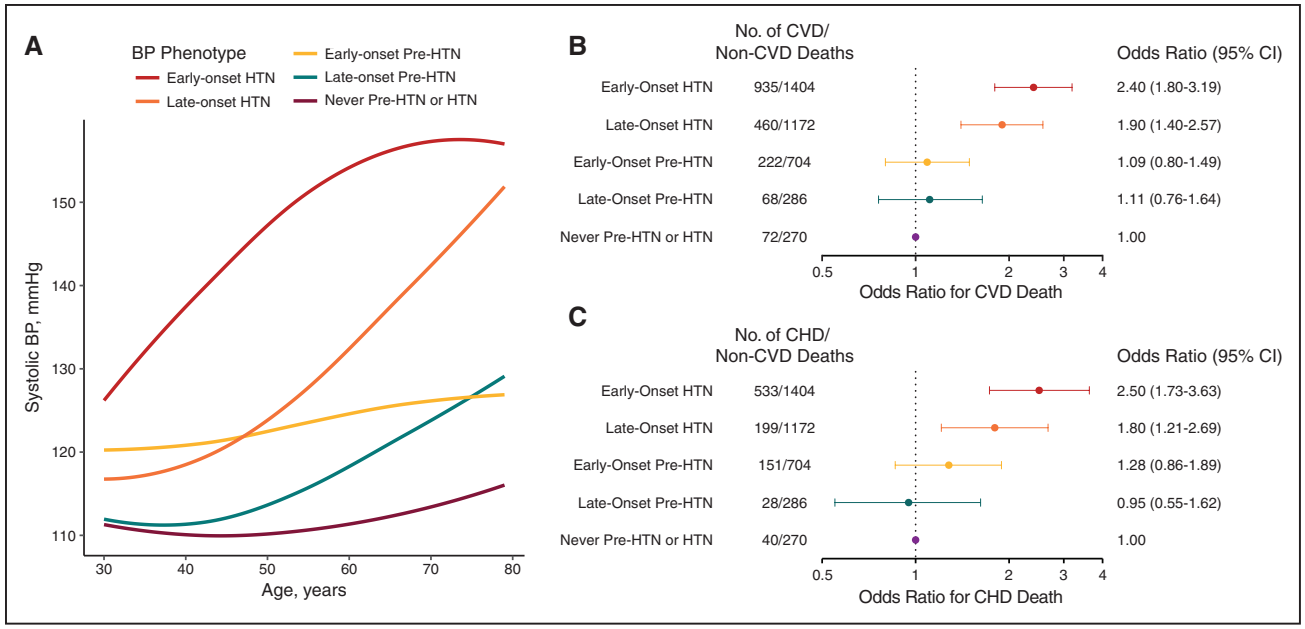

Figure. BP trajectories and associated CVD risks.
A, Mean systolic BP with increasing age by BP phenotype among decedents studied. **B** and **C,** Odds of CVD and CHD death versus non-CVD death by BP phenotype. Age at death, sex, smoking status, serum total cholesterol, cohort, and diabetes mellitus are included as covariates in the models. BP indicates blood pressure; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; and HTN, hypertension.

individuals on antihypertensive therapy) recorded at 30 to 80 years of age to illustrate longitudinal BP tracking in the 5 categories.

The mean baseline age of the sample was 42.7±7.1 (52.3% women). Mean age at death was 77.8±12.1 years. The mean BP values by age for the 5 BP phenotypes are shown in Figure A. Figure B displays the odds of CVD death and Figure C the odds of CHD death versus non-CVD death by BP phenotype. When compared with individuals who maintained optimal BP throughout life, onset of prehypertension earlier or later in life, without progression to hypertension, did not significantly increase odds of CVD death, although a trend toward increasing odds of CHD death across the 5 categories (P<0.001) did occur. By contrast, late- and especially early-onset hypertension was associated with considerably increased odds of CVD and CHD death versus other causes. We observed no interaction between BP phenotypes and cohort type with regard to odds of CVD or CHD death versus death from other causes (P≥0.43 for both). We observed similar results when analyses were repeated (1) in subgroups categorized by age at death and CVD risk level, (2) after replacing age at death as a covariate with either baseline age and follow-up length or age at entry to BP category and follow-up duration in that category, and (3) after restricting the analyses to the Original cohort (data not shown).

Progressive BP elevations can be challenging to control. In fact, ≈1/3 of middle-age prehypertensive individuals progress to hypertension over a 4-year follow-up.[2,3] Yet many prehypertensive individuals avoid developing hypertension, and we observed this phenotype to be associated with a comparably lower CVD risk relative to those who develop hypertension, even if the prehypertension develops early in life. Our results underscore the potential importance of preventing conversion from prehypertension to hypertension in the general population. Although antihypertensive therapy has been shown to reduce CVD risk by ≈15% in secondary prevention studies, data on the primary prevention of CVD with antihypertensive therapy in prehypertension are lacking.[2] Given the observational nature of our study, trials are needed to determine whether interventions aimed at preventing the progression from prehypertension to hypertension could impact longer-term outcomes among persons in the general population.

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DISCLOSURES

None.

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FOOTNOTES

The podcast and transcript are available as an online-only Data Supplement at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIRCULATIONAHA.117.029317/-/DC1.

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