Elevated blood pressure (BP) remains a widely prevalent contributor to cardiovascular risk. In the industrialized world, it has been long known that BP steadily increases with aging such that, for much of the last century, a progressively rising BP was thought to be part of the normal aging process. Evidence now indicates that age-related increases in BP are not obligatory. Indeed, little-to-no age-related increase in BP is seen in non-acculturated populations, such as the Yanomamo and Xingu Indians of Brazil, who live without exposure to vascular risk factors. Because differences in the distributions of BP are observed between populations that are genetically similar but geographically separate, the primary determinants of age-related changes in BP are likely attributed to environmental and lifestyle influences operating at least partly through traditional vascular risk factors. Nonetheless, the relationship between risk factors and longitudinal BP tracking over the life course is not well understood. Limited data suggest that the presence of risk factors in childhood may influence BP in young adulthood, but similar data in middle-aged and older adults are lacking. Such knowledge may be critical for preventing age-related increases in BP and the development of systolic hypertension in older individuals.

Previous work has established that arterial pressure can be divided into 2 main hemodynamic components: a steady state load represented by mean arterial pressure (MAP) and a pulsatile load represented by pulse pressure (PP). Whereas hypertension in younger adults commonly presents with increased diastolic BP (DBP) and MAP, hypertension in adults over 50 years of age is predominantly characterized by elevations in systolic BP (SBP) and PP, frequently presenting as isolated systolic hypertension. Accordingly, the components of BP seem to change with age in a nonlinear fashion. However, the pathophysiology underlying these nonlinear changes in BP remains unknown. Although obesity, dyslipidemia, and diabetes mellitus have been associated with various forms of hypertension, the extent to which these risk factors contribute to trajectories of BP over the adult life course is unclear.

We hypothesized that increases in the steady state and pulsatile load components of BP with aging are influenced differentially by traditional vascular risk factors. We tested this hypothesis by using multiple serial BP measurements obtained in a large community-based sample to examine how standard risk factors influence longitudinal tracking of BP and
its components over time.\textsuperscript{20–23} The ability to analyze repeated BP measures from longitudinal data offers the opportunity not only to estimate longitudinal BP tracking with relative precision but also to evaluate the influence of covariates on such tracking. Thus, we also examined differences in longitudinal tracking of BP between men and women, and determined the extent to which these sex-related differences are influenced by the presence versus absence of standard vascular risk factors.\textsuperscript{14}

**Methods**

**Study Sample**

The Framingham Offspring Study was initiated in 1971 with the enrollment of 5124 individuals composed of the children of the original Framingham Heart Study cohort and the spouses of the children. Participants of the Offspring cohort undergo routine examinations every 4 years, including a standardized assessment of cardiovascular risk factors. A total of 5124 unique participants (24208 observations) attended Offspring cohort examination cycles: 1 (1971–1975), 2 (1979–1983), 3 (1983–1987), 4 (1987–1991), 5 (1991–1995), and 6 (1995–1998). These examination cycles capture participants in young-to-middle adulthood during a contemporary time period when use of antihypertensive medications was low to moderate,\textsuperscript{24} thereby allowing us to elucidate BP tracking patterns minimally influenced by BP treatment. Of this sample, we excluded observations for individuals who were <25 or ≥75 years old at the time of any given examination (n=59 unique individuals; 1025 person-observations); a total of 59 individuals were excluded because of not meeting the age criteria at any attended examination; and, a total of 1025 observations were excluded, including for individuals who met the age criteria at ≥1 but not all examinations. In similar fashion, we also excluded from the relevant examinations any observations for individuals with prevalent myocardial infarction or heart failure (n=39; 664 observations); those with missing data on the main outcome variables, SBP or DBP (n=6; 12 observations); and those with missing data on any of the main clinical covariates for analyses (n=53; 775 observations). Thus, individuals could contribute observations to some examinations and not to others, for example, participants who developed myocardial infarction or heart failure during the follow-up period could contribute observations before the event but not afterward. In total, 4993 unique individuals providing 21732 person-examinations were included in the present analyses.

The study protocols for all examinations were approved by the institutional review board at the Boston University Medical Center. All attendees at each examination provided written informed consent.

**Clinical Assessment**

Cardiovascular risk factors, including BP, were assessed at each examination according to a standardized protocol,\textsuperscript{27} as described in detail in the online-only Data Supplement. PP was calculated as SBP–DBP; MAP was calculated as DBP+(1/3 PP). Hypertension was defined as SBP ≥140 mm Hg or DBP ≥90 mm Hg or taking antihypertensive therapy. Diabetes mellitus was defined as a fasting blood glucose value ≥126 mg/dL or the use of hypoglycemic medications.

**Statistical Analyses**

Multilevel statistical modeling allows for the analyses of data that vary at multiple levels.\textsuperscript{28} The application of multilevel modeling is particularly well suited to analyzing longitudinal data where repeated measurements, such as BP, are collected at different time points (first level) within the same individual (second level). Multilevel models allow for estimating the overall pattern of BP measurements over time, using serially collected BP measurement data, in addition to assessing the effect of clinical covariates on patterns of BP change. Unlike traditional regression models, the multilevel analytical approach provides the advantage of accommodating individuals who did not attend some of the eligible examinations and, thus, facilitates analyses that can include the maximal number of observations in a longitudinal investigation.\textsuperscript{29}

We used multilevel statistical modeling to estimate growth curves for each BP measure (SBP, DBP, MAP, and PP; separate models for each) using SAS PROC MIXED, with an unstructured correlation matrix. For individuals taking antihypertensive therapy, the previously described method\textsuperscript{30} of adding 10 mm Hg to SBP and 5 mm Hg to DBP measures was used; MAP and PP were calculated based on these imputed SBP and DBP values using the formulas noted above. To graphically demonstrate the tracking of BP measures over time, separate graphs for each BP measure were constructed for men and women.

Multilevel modeling was used to analyze the associations of each BP measure with clinical covariates that have previously been reported in relation to variation or change in BP or both: age, sex, body mass index (BMI), smoking status, diabetes mellitus, total/high-density lipoprotein (HDL) cholesterol ratio, and resting heart rate. Because all clinical covariates were assessed both at the baseline examination and at each subsequent examination, information regarding all covariate measures (including serially updated values and the timing of their measurement) was incorporated in all multivariable-adjusted multilevel models. To account for variation in BP measures between examinations, the examination cycle was included as a covariate in all analyses. Random intercepts and random effects of age were examined for all models to reflect different starting values and different slopes for age for each BP measure in each participant. To investigate possible nonlinear relations of age with each BP measure, we also examined the quadratic effect of age in all analyses (by fitting an age-squared term). We fit a series of prespecified models, constructed based on biologically plausible relationships between clinical covariates and BP measures, with direct entry of candidate variables. In addition, biologically plausible interactions among age, sex, and other clinical risk factors were investigated using corresponding interaction terms.

To illustrate the association of overall vascular risk factor burden on the patterns of BP tracking, we generated plots for both sexes based on representative high versus low risk factor status (using results of the final multivariable models). A representative high-risk status was defined as presence of all of the following: BMI=30 kg/m\textsuperscript{2}, heart rate=80 beats per minute,\textsuperscript{30} presence of diabetes mellitus, total/HDL cholesterol ratio=5,\textsuperscript{31} and being an active smoker. Similarly, a representative low-risk status was defined as presence of all of the following characteristics: BMI=25 kg/m\textsuperscript{2}, heart rate=60 beats per minute,\textsuperscript{30} absence of diabetes mellitus, total/HDL cholesterol ratio=4,\textsuperscript{31} and being a nonsmoker.

**Secondary Analyses**

We repeated all multivariable analyses in the subset of 4898 individuals without antihypertensive therapy (18658 observations). We also repeated main analyses while additionally adjusting for triglycerides, alcohol use, and the physical activity index, in the subset of 4280 individuals (16381 total observations) in whom these clinical data were available.

All analyses were performed using SAS version 9.2 and a 2-tailed \textit{P} value of <0.05 was considered significant. S-PLUS and Excel were used to create the graphical displays.

**Results**

The baseline and final examination characteristics of the study sample are shown in Table 1. Women compared with men had lower values of all BP measures at both baseline and final examinations, with the exception of PP; at the final examination, PP measures were similar between sexes. Measurements of BP were collected from a total of 21732 observations over 28 years of follow-up (Figure S1, available in the online-only Data Supplement).

On the basis of serial BP measurement data collected on the same study participants followed over time, the mean values of BP recorded at each age were plotted to depict longitudinal
BP tracking in men and women separately (Figure). As shown in unadjusted plots, SBP increased steadily with advancing age in both sexes; DBP increased and then peaked during the fifth decade and then progressively decreased in both women and men. These longitudinal profiles of SBP and DBP were accompanied by a steady increase in MAP until approximately the seventh decade, after which there was a relative plateau in MAP with increasing age. In contrast, PP

Table 1. Clinical Characteristics of the Study Participants at the First and Last Attended Examinations

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>Baseline Examination</th>
<th>Final Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (n=2408)</td>
<td>Women (n=2585)</td>
</tr>
<tr>
<td>Age, y</td>
<td>38 ± 9</td>
<td>38 ± 9</td>
</tr>
<tr>
<td>Body mass index, kg/m²²</td>
<td>26.8 ± 3.7</td>
<td>24.4 ± 4.7</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>127 ± 16</td>
<td>118 ± 17</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>82 ± 11</td>
<td>76 ± 11</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>97 ± 12</td>
<td>90 ± 12</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>45 ± 10</td>
<td>42 ± 10</td>
</tr>
<tr>
<td>Antihypertensive treatment, %</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>26</td>
<td>13</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>51</td>
<td>44</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>202.6 ± 38.9</td>
<td>193.4 ± 38.9</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>44.4 ± 12.0</td>
<td>56.4 ± 14.6</td>
</tr>
<tr>
<td>Total/HDL cholesterol</td>
<td>4.9 ± 1.7</td>
<td>3.6 ± 1.2</td>
</tr>
<tr>
<td>Triglycerides, mg/dl*†</td>
<td>150.5 ± 96.3</td>
<td>111.0 ± 68.9</td>
</tr>
<tr>
<td>Lipid lowering treatment, %</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Alcohol use, %*†</td>
<td>26</td>
<td>19</td>
</tr>
<tr>
<td>Heart rate, beats per minute</td>
<td>72 ± 13</td>
<td>78 ± 14</td>
</tr>
<tr>
<td>Physical activity index*</td>
<td>35.9 ± 6.5</td>
<td>34.0 ± 4.9</td>
</tr>
</tbody>
</table>

HDL indicates high-density lipoprotein. Values shown are mean±SD or %.
*Triglycerides, alcohol use, and physical activity index were assessed in a subsample of 2051 men and 2229 women.
†Data show alcohol intake of >14 drinks per week in men or >7 drinks per week in women.

Figure. Unadjusted mean systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and pulse pressure (PP) values with increasing age for men and women.
remained relatively constant until the fifth decade, after which PP steeply increased in both sexes.

**Clinical Correlates of BP Measures**

Over the total follow-up period, several clinical factors were positively related to progressively increasing SBP: age, male sex, BMI, diabetes mellitus, and heart rate (Table 2). In contrast, smoking status was inversely associated with SBP. In the absence of any significant interaction terms, each of these clinical correlates in the multivariable model was evaluated with respect to the relative strength of its association with longitudinal tracking of SBP. The risk factors that demonstrated the strongest associations with increasing SBP were (in decreasing order, based on values of F statistic in the model): older age, greater BMI, higher heart rate, male sex, and diabetes mellitus. Total/HDL cholesterol was not significantly associated with SBP (coefficient -0.142; \( P=0.069 \)).

Increasing DBP was positively associated with total/HDL cholesterol along with many of the same covariates associated with SBP, including age, male sex, BMI, and heart rate. Inverse correlates of DBP included diabetes mellitus as well as smoking. In addition, DBP was also inversely associated with age-squared (\( P_{\text{adj}}<0.0001 \)), reflecting a nonlinear (inverted U-shaped) pattern of DBP change with advancing age. The interaction between age and BMI was also statistically significant for DBP (\( P_{\text{adj}}<0.0001 \)), such that the relation of BMI to DBP was more prominent in younger compared with older individuals (Figure S2).

The clinical correlates of MAP generally resembled those of DBP, with the exception that MAP was not significantly associated with diabetes mellitus (coefficient -0.676, \( P=0.054 \)) (Table 2). Correlates of PP were more similar to those of SBP, with some noteworthy exceptions. Unlike for SBP, there was a statistically significant interaction between age and sex for PP, such that the increase in PP with age was greater in women than in men (\( P<0.0001 \)). A significant interaction between BMI and sex was also observed for PP, where the positive association of BMI with PP was greater in women compared with that in men (Figure S2). In addition, a higher total/HDL cholesterol ratio was associated with a lower PP, and smoking was positively associated with PP.

**Association of Risk Factor Burden on Longitudinal Tracking of BP**

Consistent with the associations described above, a representative category of high clinical risk status (ie, greater BMI, higher heart rate, presence of diabetes mellitus, active smoking history, and higher total/HDL cholesterol ratio) compared with a representative low clinical risk status (ie, normal BMI, normal heart rate, absence of diabetes mellitus and smoking, and lower total/HDL cholesterol ratio) was associated with higher BP levels over the life course (Figure S3). Both women and men with representative high-risk compared with low-risk status demonstrated higher levels of SBP, DBP, MAP, and PP from young adulthood to older age. Notably, the greater rate of rise in PP among women compared with men was similar for individuals with either high or low clinical risk burden.

**Secondary Analyses**

In multivariable analyses repeated in the subset of individuals not taking antihypertensive therapy, results were similar (Table S1). In multivariable analyses that included adjustment for additional clinical covariates, higher triglyceride levels were significantly associated with longitudinal increase in BP measures (all \( \beta \)s are in mm Hg per SD increment in triglycerides): SBP (\( \beta=0.877; P<0.0001 \)), DBP (\( \beta=0.178; P=0.017 \)), MAP (\( \beta=0.307; P=0.0002 \)), and PP (\( \beta=0.511; P<0.0001 \)). Moderate or greater alcohol consumption use was also associated with increase in all BP outcomes (\( \beta \)s in mm Hg):

**Table 2. Clinical Correlates of Longitudinal Tracking of Change in SBP, DBP, MAP, and PP**

<table>
<thead>
<tr>
<th>Baseline Covariates</th>
<th>SBP Coefficient (SE)</th>
<th>P Value</th>
<th>DBP Coefficient (SE)</th>
<th>P Value</th>
<th>MAP Coefficient (SE)</th>
<th>P Value</th>
<th>PP Coefficient (SE)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 y)</td>
<td>6.566 (0.182)</td>
<td>&lt;0.0001</td>
<td>4.159 (0.357)</td>
<td>&lt;0.0001</td>
<td>4.132 (0.126)</td>
<td>&lt;0.0001</td>
<td>4.656 (0.160)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-squared</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Male sex</td>
<td>6.425 (0.350)</td>
<td>&lt;0.0001</td>
<td>4.129 (0.223)</td>
<td>&lt;0.0001</td>
<td>4.743 (0.256)</td>
<td>&lt;0.0001</td>
<td>6.241 (1.219)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI (per 5 kg/m²)</td>
<td>5.084 (0.155)</td>
<td>&lt;0.0001</td>
<td>3.362 (0.097)</td>
<td>&lt;0.0001</td>
<td>4.212 (0.110)</td>
<td>&lt;0.0001</td>
<td>1.739 (0.134)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoking</td>
<td>−0.724 (0.249)</td>
<td>0.004</td>
<td>−1.191 (0.156)</td>
<td>&lt;0.0001</td>
<td>−0.965 (0.173)</td>
<td>&lt;0.0001</td>
<td>0.557 (0.184)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2.145 (0.534)</td>
<td>&lt;0.0001</td>
<td>−1.124 (0.311)</td>
<td>0.003</td>
<td>...</td>
<td>...</td>
<td>4.571 (0.406)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total/HDL cholesterol (per 2 units)</td>
<td>...</td>
<td>...</td>
<td>0.469 (0.095)</td>
<td>&lt;0.0001</td>
<td>0.275 (0.105)</td>
<td>0.009</td>
<td>−0.719 (0.115)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart rate (per 10 bpm)</td>
<td>1.655 (0.085)</td>
<td>&lt;0.0001</td>
<td>1.100 (0.053)</td>
<td>&lt;0.0001</td>
<td>1.135 (0.058)</td>
<td>&lt;0.0001</td>
<td>0.795 (0.064)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Note:** BP indicates blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; BMI, body mass index; HDL, high-density lipoprotein; bpm, beats per minute. Age was centered at the mean of all participants at all examinations (49 years) to reduce multicollinearity between regression coefficients. All models were also adjusted for examination cycle. The regression coefficients represent the change in mean SBP, DBP, PP, or MAP (in mm Hg) per corresponding unit increase in the continuous covariates (or presence vs absence of categorical covariates). Note that main effects of covariates are not directly interpretable in the presence of cross-product terms evaluating interactions.
SBP (β=2.816; P<0.0001), DBP (β=1.471; P<0.0001), MAP (β=2.028; P<0.0001), and PP (β=1.385; P<0.0001). Physical activity was not significantly related to either SBP (P=0.39) or MAP (P=0.26). However, physical activity was modestly related to increased DBP (β=0.174 mm Hg per 1-SD increment in physical activity index; P=0.015), in a direction that was consistent with the proportionately greater decrease in PP that was observed in association with physical activity (β=−0.297 mm Hg per 1-SD increment in physical activity; P=0.001).

Discussion

Previous investigations of age-related trends in BP have been limited to cross-sectional or group averaged data.5,10,13 By applying a multilevel modeling approach to analyze both intra- and inter-individual BP measurements over serial time points, we were able to delineate BP tracking over the life course and also identify risk factor correlates. Our data confirm an overall pattern of age-related change in BP that is characterized by steady increases in SBP and DBP in early adulthood, followed by a steeper increase in SBP and marked decrease in DBP in later life. Accordingly, we observed that MAP steadily increases throughout adulthood until reaching a relative plateau in the seventh decade of life, somewhat later than suggested by previous studies10; conversely, PP begins to increase at about 40 years of age, after which PP continues to steeply rise throughout the remaining life course.

Several established risk factors for hypertension were associated with longitudinal increase in all BP measures. These risk factors included increased heart rate32,33 and greater BMI,34,35 with similar results observed for triglycerides36,37 and moderate alcohol consumption in the subgroup with available data on these variables.38,39 We observed that age and sex influenced the association of BMI with select BP indices. Notably, the association of greater BMI with higher DBP was more prominent in younger compared with older adults, raising the possibility that larger body size in early life is associated with small vessel resistance in the absence of the large vessel remodeling that more typically occurs in older age.40 The relationship between BMI and PP was more prominent in women than in men, consistent with cross-sectional reports41 and potentially related to sex-based anatomic limits in the extent to which arterial diameter can increase along with BMI, reflecting the arterial remodeling responses to excess adiposity.

Not all risk factors were associated with similar increases in all BP outcomes over the life course. Diabetes mellitus was associated with measures of pulsatile rather than steady state arterial load. Cross-sectional studies have related diabetes mellitus to arterial stiffness42,43 and the preferential stiffening of the central over peripheral arteries in particular.44 Diabetes mellitus may promote large artery stiffening through the formation of advanced glycation end products, causing cross-linking of collagen along the arterial wall.43,44 Although some cross-sectional studies have suggested that the relationship between diabetes mellitus and BP indices may be more pronounced in women than in men,43 we did not observe a sex interaction in our longitudinal analyses. In contrast to diabetes mellitus, total/HDL cholesterol was directly associated with BP measures of steady state and inversely with pulsatile load.

Despite being a recognized risk factor for hypertension,46 the extent to which hypercholesterolemia affects the hemodynamic components of BP has previously been unclear. Studies exploring the possibility that serum cholesterol is a stronger determinant of small versus large vessel resistance have thus far yielded conflicting results.47–50

Longitudinal patterns of BP tracking were consistently more pronounced in women than in men. Women experienced an earlier rise in SBP and PP with age and a slightly later decrease in DBP with a corresponding later plateau in MAP. Notably, age-related increase in PP was higher in women than in men, corresponding with differences in PP that were observed between women and men at the baseline but not at the final examinations. Sexual dimorphism in BP tracking is likely related to factors that precede as well as accompany the menopausal transition.51,52 Small observational and experimental studies indicate that young, premenopausal women have lower autonomic tone53,54 and baroreceptor response54 than men of similar age. Additionally, women have higher forward and reflected wave amplitude than men on arterial tonometry, manifesting more frequently as aortic stiffness.55 Together with previous work, our findings suggest that although women may initially have lower BP measures than men overall, they tend to experience greater pulsatile load with advancing age. This effect could be exacerbated by greater coupling of ventricular and vascular stiffening with aging and in the setting of smaller sized vessels in women compared with men.56 Notably, a higher versus lower clinical risk profile, defined by the presence of traditional determinants of hypertension, conferred similar increases in all BP measures that were comparable between the sexes.

Several limitations of our investigation merit consideration. Because data regarding serum triglycerides, alcohol use, and physical activity were available for only a subset of the total sample, these covariates were included in secondary analyses only. Given the long follow-up duration required for our study design, baseline data were collected up to several decades ago; thus, the generalizability of our findings to individuals with elevated BP in the contemporary era and to recent birth cohorts (with different sets of environmental exposures) is not known. Our study sample was predominantly comprised of white individuals of European ancestry and, thus, the extent to which our findings are generalizable to other racial/ethnic groups is also unknown. Notwithstanding these limitations, our study had several strengths. Our investigation included a large, community-based sample followed closely with serial BP measurements over 3 decades. This longitudinal design permitted the use of a multilevel modeling analytical approach, which facilitates the evaluation of serial BP measures within and between individuals as well as the correlates of longitudinal alterations in BP indices. Because our findings are based on observational data, they may be considered hypothesis generating.

Perspectives

We observed that longitudinal BP changes with aging are characterized by distinct patterns of increase in SBP, DBP, MAP, and PP. These patterns begin in young adulthood, span several decades, and are influenced to varying degrees by the presence of select vascular risk factors. Although many risk factors are related to longitudinal increase in all BP
measures, dyslipidemia is particularly related to increase in steady state load, whereas diabetes mellitus and smoking are more strongly associated with elevations in pulsatile load. Additionally, women are more predisposed than men to higher pulsatile load over the life course. Further research is needed to investigate the mechanisms underlying these observations and, in turn, the extent to which targeted interventions can attenuate the typical trajectory of BP progression with aging.

Sources of Funding

This work was supported by the Ellison Foundation (Dr Cheng); the National Heart, Lung, and Blood Institute’s Framingham Heart Study (Contract No. N01-HC-25195); and the following grants: K99HL107642 (Dr Cheng) and R01HL080124 (Dr. Vasan).

Disclosures

None.

References


Downloaded from http://hyper.ahajournals.org/ by guest on October 30, 2017


---

**Novelty and Significance**

**What Is New?**

- Although it is well known that BP steadily increases with age, the extent to which risk factors influence age-related elevations in BP is unclear.

**What Is Relevant?**

- Elevated BP remains a major lifetime contributor to cardiovascular disease.
- Understanding how risk factors may impact trajectories of BP over the life course is needed to prevent age-related increases in BP.

**Summary**

- Select vascular risk factors differentially impact the longitudinal tracking of individual components of BP.
- Further research is needed to investigate the mechanisms that regulate BP components over the life course, and their potential as targets for preventing age-related BP progression.
Blood Pressure Tracking Over the Adult Life Course: Patterns and Correlates in the Framingham Heart Study

Susan Cheng, Vanessa Xanthakis, Lisa M. Sullivan and Ramachandran S. Vasan

Hypertension. 2012;60:1393-1399; originally published online October 29, 2012; doi: 10.1161/HYPERTENSIONAHA.112.201780

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/60/6/1393

Data Supplement (unedited) at:
http://hyper.ahajournals.org/content/suppl/2012/10/29/HYPERTENSIONAHA.112.201780.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/
Blood Pressure Tracking Over the Adult Life Course:

Patterns and Correlates in the Framingham Heart Study

Susan Cheng, MD, Vanessa Xanthakis, PhD, Lisa M. Sullivan, PhD,
Ramachandran S. Vasan, MD

ONLINE SUPPLEMENT

From the Framingham Heart Study (S.C., V.X., R.S.V.), Framingham, MA; Division of Cardiovascular Medicine (S.C.), Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; Department of Biostatistics (V.X., L.M.S.), Boston University School of Public Health, Boston, MA; and, Preventive Medicine (V.X., R.S.V.) and Cardiology (R.S.V.) Sections, Boston University School of Medicine, Boston, MA.

Correspondence: Susan Cheng, MD, Cardiovascular Division, Brigham and Women’s Hospital, 75 Francis Street, PBB-119, Boston, MA 02115, phone (857) 307-1960, fax (617) 812-0425, email scheng3@partners.org; Ramachandran S. Vasan, MD, The Framingham Heart Study, 73 Mount Wayte Ave, Suite 2, Framingham, MA 01702–5803, phone (508) 935-3450, fax (508) 626-1262, email vasan@bu.edu.

Short title: Blood pressure tracking over the life course

Total word count: 5,948
METHODS

Clinical Assessment
At each examination, according to a standardized protocol,\textsuperscript{1} systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice in the left arm of seated participants who had been resting for at least 5 minutes; the average of the two readings was used as the examination BP. Fasting blood specimens were collected for cholesterol and glucose assays.\textsuperscript{2} Diabetes mellitus was defined as a fasting blood glucose level of ≥126 mg/dL or the use of hypoglycemic medications. Physical activity assessment was based on a physical activity index, calculated from the reported number of hours spent per day at varying activity levels, which were weighted according to the estimated oxygen consumption required for each activity.\textsuperscript{3} Alcohol use was dichotomized as moderate or more, defined as the consumption of >14 alcoholic drinks per week in men or >7 alcoholic drinks per week in women.

Blood Pressure Variables
Pulse pressure (PP) was calculated as SBP minus DBP, and mean arterial pressure (MAP) was calculated as DBP plus 1/3 PP. Across all observations (N=21,732), correlations between the BP indices demonstrated the expected direction and magnitude: SBP was strongly correlated with both MAP and PP with age- and sex-adjusted Pearson correlation coefficients of $r=0.92$ ($p<0.0001$) and $r=0.81$ ($p<0.0001$), respectively; DBP was strongly correlated with MAP ($r=0.94$; $p<0.0001$) and modestly with PP ($r=0.18$; $p<0.0001$).

REFERENCES


Table S1. Clinical correlates of longitudinal tracking of change in SBP, DBP, MAP, and PP among individuals not on any antihypertensive therapy.

<table>
<thead>
<tr>
<th>BP Components</th>
<th>SBP</th>
<th></th>
<th>DBP</th>
<th></th>
<th>Steady-State Load</th>
<th></th>
<th>Pulsatile Load</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient (SE)</td>
<td>P value</td>
<td>Coefficient (SE)</td>
<td>P value</td>
<td>Coefficient (SE)</td>
<td>P value</td>
<td>Coefficient (SE)</td>
<td>P value</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>5.735 (0.179)</td>
<td>&lt;0.0001</td>
<td>3.253 (0.385)</td>
<td>&lt;0.0001</td>
<td>3.744 (0.124)</td>
<td>&lt;0.0001</td>
<td>4.224 (0.159)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-squared</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Male Sex</td>
<td>6.839 (0.334)</td>
<td>&lt;0.0001</td>
<td>4.441 (0.219)</td>
<td>&lt;0.0001</td>
<td>5.194 (0.247)</td>
<td>&lt;0.0001</td>
<td>6.339 (1.225)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age * Male Sex</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>BMI (per 5 kg/m²)</td>
<td>4.901 (0.154)</td>
<td>&lt;0.0001</td>
<td>3.265 (0.127)</td>
<td>&lt;0.0001</td>
<td>4.108 (0.110)</td>
<td>&lt;0.0001</td>
<td>1.672 (0.136)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age * BMI</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Male Sex * BMI</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Current smoking</td>
<td>-0.819 (0.243)</td>
<td>0.001</td>
<td>-1.257 (0.157)</td>
<td>&lt;0.0001</td>
<td>-1.075 (0.170)</td>
<td>&lt;0.0001</td>
<td>0.551 (0.183)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.552 (0.608)</td>
<td>&lt;0.0001</td>
<td>-1.648 (0.368)</td>
<td>0.078</td>
<td>—</td>
<td>—</td>
<td>4.209 (0.460)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total/HDL cholesterol (per 2 units)</td>
<td>—</td>
<td>—</td>
<td>0.295 (0.098)</td>
<td>0.003</td>
<td>0.089 (0.106)</td>
<td>0.40</td>
<td>-0.648 (0.117)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart rate (per 10 bpm)</td>
<td>2.003 (0.084)</td>
<td>&lt;0.0001</td>
<td>1.223 (0.055)</td>
<td>&lt;0.0001</td>
<td>1.134 (0.058)</td>
<td>&lt;0.0001</td>
<td>1.028 (0.065)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial pressure; BMI, body mass index; HDL, high-density lipoprotein; bpm, beats per minute. Age was centered at the mean of all participants at all exams (49 years) to reduce multi-collinearity between regression coefficients. All models also adjusted for examination cycle. The regression coefficients represent the change in mean SBP, DBP, PP, or MAP (in mmHg) per corresponding unit increase in the continuous covariates (or presence versus absence of categorical covariates). Note that main effects of covariates are not directly interpretable in the presence of cross-product terms evaluating interactions.
Figure S1. Study design. Longitudinal tracking of BP measurements was performed in 4,933 unique individuals who attended up to 6 serial examinations, contributing a total of 21,732 observations.
Figure S2. Unadjusted mean diastolic blood pressure (for ages below and above 50 years) and pulse pressure (for men and women) values with increasing body mass index.
Figure S3. Adjusted mean values of SBP, DBP, MAP, and PP with increasing age were illustrated in men and women, separately, and by high versus low clinical risk group. Higher clinical risk was defined as having a BMI of 30 kg/m², heart rate of 80 beats per minute, presence of diabetes, active smoking history, and total/HDL cholesterol ratio of 5, compared to low clinical risk, i.e. BMI of 25 kg/m², heart rate 60 beats per minute, absence of diabetes and smoking, and a total/HDL cholesterol ratio of 4.