Mid- to Late-Life Trajectories of Blood Pressure and the Risk of Stroke
The Rotterdam Study

Marileen L.P. Portegies, Saira Saeed Mirza, Vincentius J.A. Verlinden, Albert Hofman, Peter J. Koudstaal, Sonja A. Swanson, M. Arfan Ikram

Abstract—Hypertension is a major modifiable risk factor for stroke. Associations of blood pressure with incident stroke are mostly based on single or average blood pressure levels. However, this approach does not take into account long-term trajectories of blood pressure, which can vary considerably in the elderly. Within the population-based Rotterdam Study, we examined trajectories of systolic blood pressure in 6745 participants (60.0% women) over an age-range from 55 to 106 years and jointly modeled their risk of stroke and competing causes of death using joint latent class mixed modeling. Four trajectories were identified. Class 1 was characterized by blood pressure increasing gradually from an average 120 to 160 mmHg over 5 decades (n=4938). Compared with this class, class 2, characterized by a similar midlife blood pressure, but a steep increase (n=822, increasing from 120 to 200 mmHg), and class 4, characterized by a high midlife blood pressure (n=115; average 160 mmHg) and had a higher risk of stroke and death. Class 3, characterized by a moderate midlife blood pressure (n=870; average 140 mmHg), had a similar risk of death as class 1, but the highest risk of stroke. Assessing trajectories of blood pressure provides a more nuanced understanding of the associations between blood pressure, stroke, and mortality. In particular, high blood pressure and rapidly increasing blood pressure patterns are associated with a high risk of stroke and death, whereas moderately high blood pressure is only related to an increased risk of stroke. Future studies should explore the potential pathogenic significance of these patterns. (Hypertension. 2016;67:1126-1132. DOI: 10.1161/HYPERTENSIONAHA.116.07098.) ● Online Data Supplement

Key Words: blood pressure ● epidemiology ● hypertension ● mortality ● stroke

Hypertension is a major treatable risk factor for stroke, with an estimated attributable risk of 35% to 50%.12 Most studies that examined the association between hypertension and incident stroke used a single measurement or the average of blood pressure levels assessed over time. Results from such approaches have suggested that the risk of stroke increases with increasing blood pressure levels and that even prehypertension is associated with stroke.4,8 Indeed, the current guideline to treat people above a certain target level of blood pressure (eg, 150/90 mmHg7 or 140/90 mmHg8–10) is largely based on such knowledge. However, long-term patterns (ie, trajectories) of blood pressure may further influence stroke risk. Studies in young- and middle-aged adults showed that increases in blood pressure over long periods (10–30 years) are related to an increased risk of stroke and cardiovascular disease,11–13 and that trajectories of higher blood pressure relate to a higher risk of subclinical atherosclerosis.14 Trajectories in older people may vary even more because it is particularly in later ages that arterial stiffness increases, which is associated with increases in blood pressure and blood pressure variability.15–17 Furthermore, studies suggest that lower blood pressures might also be harmful in this population, leading to an increased risk of myocardial infarction or death.18–20 This has particularly been observed for low diastolic blood pressures18,19 although low systolic blood pressures (SBPs) also seemed to be harmful in patients with vascular disease and diabetes mellitus.20 To date, no study of long-term blood pressure trajectories in mid- to late-life has been conducted. Furthermore, it is unknown whether such trajectories relate to stroke. If we hope to empirically inform and refine prevention guidelines, a much-needed first step is to describe the prototypic and commonly observed patterns of blood pressure trajectories.

Therefore, the aim of our study was to identify long-term trajectories of blood pressure in a population-based study and to examine the risk of stroke within those trajectories. We focused on SBP because it is the best predictor of cardiovascular events.21

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Methods

Setting and Study Population
This study was conducted within the prospective, population-based Rotterdam Study. Details on the objectives and design of the study have been described elsewhere.22 Baseline examinations started in 1990 among 7983 people of ≥55 years residing in Ommoord, a suburb of Rotterdam, the Netherlands. Follow-up examinations take place every 3 to 4 years.

For the current study, data from 5 follow-up visits from 1990 to 2011 were used. Participants with no informed consent for follow-up data collection (n=226), prevalent stroke at baseline (n=243), no center visit prior to a stroke (n=668), and completely missing information on blood pressure and blood pressure–lowering medication (n=101) were excluded, resulting in 6745 participants eligible for the current analysis. Only measurements before occurrence of stroke were used. We had 6679, 5018, 3570, 2891, and 1499 measurements at each of the 5 center visits, respectively, totaling 19,657 measurements.

The Rotterdam Study has been approved by the Medical Ethics Committee of the Erasmus MC and by the Ministry of Health, Welfare and Sport of the Netherlands, implementing the Wet Bevolkingsonderzoek: ERGO (Population Studies Act: Rotterdam Study). All participants provided written informed consent to participate in the study and to obtain information from their treating physicians.

Assessment of Blood Pressure
During each visit, blood pressure was measured twice in the right arm, in sitting position, after a resting period of 5 minutes. The average of the 2 measurements was used in the analyses. Until November 7, 2006, a Hawksley random-zero sphygmomanometer was used,23 and for measurements after this date Omron M6 Comfort and Omron M7 devices were used.24,25

Assessment of Stroke
Stroke was defined according to WHO criteria as a syndrome of rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting ≥24 hours or leading to death and no apparent cause other than of vascular origin.26 This corresponds to International Classification of Diseases-Tenth Revision codes I61, I63, and I64. At baseline, history of stroke was assessed by interview and verified using medical records.27 Subsequently, participants were continuously followed up for occurrence of incident stroke, by digital linkage of the general practitioners’ medical records with the study database. Nursing home physicians’ medical records and general practitioners’ medical records of participants who moved out of the Ommoord district were checked on a regular basis as well. Of all potential strokes, medical records from general practitioners and hospital discharge letters were collected and reviewed by research physicians. An experienced vascular neurologist verified the diagnoses. Follow-up through January 1, 2013, was complete for 98.9% of potential person-years.28

Covariates
Covariates were assessed at each center visit. Details on the assessment of anthropometrics, cardiovascular risk factors (total cholesterol, high-density lipoprotein cholesterol, diabetes mellitus type 2, and smoking), and the use of medication have been described previously.29 Current alcohol use was assessed during each home interview and categorized into yes versus no. The use of blood pressure–lowering medication included the use of diuretics, β-blocking agents, calcium blockers, angiotensin receptor blockers, and angiotensin-converting enzyme-inhibitors if prescribed for the indication hypertension. The second center visit had limited examinations, and in particular had no assessment of cholesterol, high-density lipoprotein cholesterol, and diabetes mellitus status. Therefore, measurements from the preceding center visit were carried forward.

Statistical Analysis
We investigated the association of longitudinal trajectories in SBP over age with the risk of stroke using a joint latent class mixed model. The main goal of a joint latent class mixed model is to describe the link between a continuous progression of diseases through longitudinal markers such as blood pressure, and the incidence of clinical events.30,31 The model uses all available information from the blood pressure and outcome measurements to model trajectories and co-occurring events like stroke and death.30,31 Because hypertension has been associated with both ischemic and hemorrhagic strokes,32 we examined the risk with all stroke types. Models were fit using the jointlcmm function of the lcmm package in R.33 The joint latent class mixed model assumes that people’s blood pressure trajectories cluster in a set of mutually exclusive patterns or latent classes. That is, there are prototypical patterns in blood pressure trajectories that individuals follow. In the current analysis, the model differentiates the population into groups (latent classes) with different profiles of blood pressure and links these classes to potential risk of stroke.30,31,33 Trajectories of blood pressure over age from 55 years onward were modeled using a class-specific linear mixed model with age as time.30 Because blood pressure may have a nonlinear pattern, we also added a class-specific quadratic age term. We included random intercepts and random slope in all analyses. We added class-specific adjustments for sex and baseline blood pressure–lowering medication because we expected these variables may influence the evolution of blood pressure. People entered at study baseline and were censored at date of stroke, date of death, last date of follow-up or January 1, 2013, whichever came first. The optimal number of classes was defined by the model with the lowest Bayesian information criterion.34 Analyses were repeated using different random starting values to ensure convergence to the global maximum of the model.35 We were primarily interested in stroke as outcome, but added stroke-free mortality because it is an important competing risk. The joint survival model was therefore defined by a 2-parameter Weibull distribution with a class-specific baseline risk function for both stroke and the competing risk of mortality because of any other cause than stroke.30,31 This includes cardiovascular deaths. The survival function was adjusted for sex and blood pressure–lowering medication, and in the multivariable model, we additionally adjusted for visit-specific cholesterol, high-density lipoprotein cholesterol, lipid-lowering medication, body mass index, smoking, alcohol use, diabetes mellitus type 2, and antithrombotic medication. Adjustments in the survival part of the analysis were only made for baseline characteristics. However, we do provide characteristics of later visits, to compare the evolution of these characteristics together with blood pressure. ANCOVA was used to study differences in baseline characteristics between participants within the different estimated trajectory classes, adjusted for age and sex. Covariates were missing for up to a maximum of 4.6% across assessments. Missing values were imputed by the mean of 5 imputations, using multiple imputation based on the other covariates of the same visit. Class-specific trajectories of blood pressure or cumulative incidences of stroke or death were estimated for the mean value for all covariates. A Monte Carlo method was used to calculate the confidence intervals of the cumulative incidences.32

Sensitivity Analyses
Sensitivity analyses were conducted to explore the robustness of our results to modeling decisions, missing data, and censorship. First, we inspected models based on 1 fewer and 1 greater trajectory than the model chosen based on lowest Bayesian information criterion. Second, we added a cubic age term. Third, to understand the robustness of our observed patterns to missing values and censoring for stroke or death in between the measurements, we repeated our analyses based on data from only the first 3 visits (from 1989 to 1999) in the people without missing values in these visits and examined the survival curves thereafter (from 1999 to 2013). Fourth, because few participants were alive and stroke free after the age of 80 years, we wanted to understand whether our identified trajectories were similar in only younger ages. Therefore, we also repeated analyses in which we only included SBP measurements assessed between the ages of 55 and 80 years. Finally, although latent class modeling is a useful data-reduction tool for understanding general patterns, individual membership in a class
or trajectory is probabilistic. As a posterior check to see how observed trajectories of blood pressure of individual participants aligned with the identified trajectories in our final model, as well as to visually assess missing data patterns, we plotted the individual blood pressure values by most likely trajectory class, visit, outcome, and age.16

Results

Characteristics of the Trajectory Classes
Participants had a mean (±SD) follow-up of 13.5±6.8 years, during which 1053 strokes occurred.

When investigating the trajectories, we found that the joint latent class model with 4 classes had the best fit, with the lowest Bayesian information criterion (Table S1 in the online-only Data Supplement). Mean posterior class membership probabilities (ie, the probability that a person belongs to his or her most likely class) were ≥63% for each class in this model. Figure 1A shows the 4 identified trajectories of SBP, based on the joint latent class mixed model. The largest class was characterized by a gradually increasing blood pressure, starting at ≈120 mmHg at the age of 55 years and increasing up to ≈160 mmHg at the age of 95 years (class 1, n=4938). A smaller class was characterized by a similar blood pressure at the age of 55 years, but a much steeper increase up to ≈200 mmHg (class 2, n=822). Two classes were characterized by a relatively higher baseline blood pressure: one of ≈140 mmHg, with modest variation over time (class 3, n=870), and the other of ≈160 mmHg, which decreased after age 65 (class 4, n=115). Figure S1 shows the model-based trajectories compared with the mean observed values in the classes. The predicted values only diverge slightly from the observed values in people at old age. For instance, the observed values of the high baseline SBP class plateau at old age, whereas the predicted trajectory continues to increase.

People in class 4 were more frequently men (Table). Mean and maximum baseline blood pressure assessments were highest in class 4 followed by the class 3 and class 2. The use of blood pressure–lowering medication was similar between classes at baseline, but at the end of follow-up, the class 3 and class 4 had higher proportions of blood pressure–lowering medication users. Values on other covariates at each study visit are presented in Table S2. We found a large difference in frequency of current smokers among classes, with particularly higher frequencies in class 2 and class 4.

Risk of Stroke and Death for the Separate Trajectories
Relative to class 1, the increased risk of stroke was apparent in class 4 beginning at the age of 55 years onward, whereas increased stroke risk began later (age, ≈65 years) for classes 2 and 3 (Figure 1B). The 3 classes had a significantly and substantially higher risk of stroke than class 1 (eg, 4.7%–13.6% compared with 0.7%). The estimated risks up to the age of 75 years seemed higher in class 4 (13.6%) than in classes 2 (8.1%) and 3 (4.7%) although the wide confidence intervals limited interpretability (Table S3). Classes 2 and 4 also had the highest risk of dying through other causes (Figure 1C). The cumulative incidence curves in those classes plateaued around ages 75 to 85 years, at that time roughly all people in the classes were diagnosed as having a stroke or died. The risk of stroke in class 3 continued to increase until older age. However, the risk of dying was lower than in class 2 and 4, similar to class 1.

At the end of follow-up, 2546 people (51.5%) in class 1, 575 (70.0%) people in class 2, 288 (33.1%) people in class 3, and 87 (75.7%) people in class 4 died because of a nonstroke-related cause. Between 25% and 38% of nonstroke deaths in each class were because of cardiovascular events (Figure S2).

Multivariable-adjusted models were relatively similar although some people’s most probable class membership switched. Risks of stroke in class 2 and 4 attenuated, whereas the risk became stronger in class 3 (Figure 2).

Sensitivity Analyses
Visual assessment of individual blood pressure patterns by participants’ most likely class membership, visit, age, and outcome suggested that the model-based patterns were unlikely to be influenced by missing data and that the described trajectories reflected observable patterns within and across individuals (Figure S2). On the contrary, differences in blood pressure over time seen between classes 1 and 2 were mainly apparent.
in older people. Furthermore, people assigned to class 4 often had a stroke or death at young age, with few people within this class having decreases in blood pressure, suggesting that the model-estimated decrease in this trajectory may be an artifact of a small number of survivors.

The 3- and 5-class model did not provide any additional insights. In the 3-class model, no class resembling class 4 was identified. In the 5-class model, the class resembling class 4 with respect to the high midlife blood pressure was further subdivided into a class that was increasing and a class that was decreasing. For classes that heuristically overlapped with those identified in the 4-class models, patterns of stroke and mortality risk were similar. The class with a high midlife blood pressure that was increasing, was related to both stroke and death, whereas the class with a high midlife blood pressure that was decreasing, was associated only with death; for both classes, numbers were low.

In the sensitivity analysis in which we only included people that completed the 3 first visits of blood pressure measurement, trajectories of blood pressure remained similar. Furthermore, we found a similar risk of death in the different classes. The risk of stroke was highest in class 3, followed by class 2. Class 4 did not have an increased risk of stroke (Figure S3).

In another sensitivity analysis in which trajectories were formed based only on measurements at the ages of 55 to 80 years only, trajectories and associated risks of stroke were similar to our main findings (Figure S4).

We report the results of trajectories that only allowed for a quadratic effect of age over time. As sensitivity analysis we did add a cubic age term, but this did not provide any additional insight (Figure S5).

Discussion

In this population-based study of people aged ≥55 years, we identified 4 trajectories of blood pressure: a class characterized by a gradually increasing blood pressure from ≈120 to 160 mm Hg (on average) over 5 decades (class 1); a class characterized by a more steep increase from an average of ≈120 to 200 mm Hg (class 2); a class characterized by a moderate blood pressure (≈140 mm Hg) at midlife and throughout (class 3); and a class characterized by a high blood pressure (≈160 mm Hg) at midlife that decreased (class 4). The class with a high blood

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Class 1 (n=4938)</th>
<th>Class 2 (n=822)</th>
<th>Class 3 (n=870)</th>
<th>Class 4 (n=115)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at entry, y</td>
<td>71.0 (9.4)*,†,‡</td>
<td>64.5 (6.0)†,‡,§</td>
<td>65.7 (7.1)*,†,‡,§</td>
<td>62.0 (5.0)*,†,‡,§</td>
</tr>
<tr>
<td>Women</td>
<td>3017 (61.1%)‡</td>
<td>470 (57.2%)‡</td>
<td>511 (58.7%)‡</td>
<td>48 (41.7%)*,†,‡,§</td>
</tr>
<tr>
<td>Mean systolic blood pressure, mm Hg</td>
<td>140 (17%)*,†,‡</td>
<td>148 (22%)*,†,‡,§</td>
<td>162 (14%)*,†,‡,§</td>
<td>167 (20%)*,†,‡,§</td>
</tr>
<tr>
<td>Maximum systolic blood pressure, mm Hg</td>
<td>152 (20%)*,†,‡</td>
<td>161 (29%)*,†,‡,§</td>
<td>177 (17%)*,†,‡,§</td>
<td>184 (20%)*,†,‡,§</td>
</tr>
<tr>
<td>Use of blood pressure-lowering medication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entry</td>
<td>1003 (20.5%)*,†,‡</td>
<td>223 (27.4%)§</td>
<td>220 (25.5%)§</td>
<td>27 (24.1%)§</td>
</tr>
<tr>
<td>End</td>
<td>1686 (34.1%)*,†,‡</td>
<td>271 (33.0%)†,‡,§</td>
<td>508 (58.4%)*,§</td>
<td>71 (61.7%)*,§</td>
</tr>
<tr>
<td>Characteristics at visit 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean systolic blood pressure, mm Hg</td>
<td>135 (20%)*,†,‡</td>
<td>142 (23%)*,†,‡,§</td>
<td>158 (20%)*,†,‡,§</td>
<td>174 (20%)*,†,‡,§</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>1997 (41.9%)*,†,‡</td>
<td>310 (38.9%)†,‡,§</td>
<td>385 (45.1%)*,‡,§</td>
<td>51 (45.9%)*,†,‡,§</td>
</tr>
<tr>
<td>Current</td>
<td>974 (20.4%)*,†,‡</td>
<td>286 (35.9%)*,†,‡,§</td>
<td>170 (19.9%)*,†,‡,§</td>
<td>47 (42.3%)*,†,‡,§</td>
</tr>
<tr>
<td>Current use of alcohol</td>
<td>2940 (78.7%)</td>
<td>565 (81.5%)</td>
<td>588 (79.7%)</td>
<td>84 (84.0%)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>6.6 (1.2)†</td>
<td>6.7 (1.2)†</td>
<td>6.8 (1.2%)*,§</td>
<td>6.7 (1.1)</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol, mmol/L</td>
<td>1.4 (0.4)</td>
<td>1.3 (0.4)</td>
<td>1.4 (0.4)</td>
<td>1.3 (0.4)</td>
</tr>
<tr>
<td>Use of lipid-lowering medication</td>
<td>102 (2.1%)</td>
<td>21 (2.6%)</td>
<td>30 (3.5%)</td>
<td>3 (2.7%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>336 (7.4%)*,†,‡,§</td>
<td>57 (7.4%)*,†,‡,§</td>
<td>63 (7.6%)*,†,‡,§</td>
<td>14 (13.0%)*,†,‡,§</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.2 (3.7)*,†,‡</td>
<td>26.1 (3.8)*,†,‡</td>
<td>26.8 (3.6)*,‡,§</td>
<td>27.1 (3.7%)*,‡,§</td>
</tr>
<tr>
<td>Use of antithrombotic medication</td>
<td>224 (4.6%)*</td>
<td>46 (5.7%)*,†,‡,§</td>
<td>30 (3.5%)*</td>
<td>2 (1.8%)*</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD) or counts (percentages).
*Compared with class 2, P<0.05 after age and sex adjustment if applicable.
†Compared with class 3, P<0.05 after age and sex adjustment if applicable.
‡Compared with class 4, P<0.05 after age and sex adjustment if applicable.
§Compared with class 1, P<0.05 after age and sex adjustment if applicable.
pressure at midlife and the class with a steep increase had the highest risks of stroke and death through the age of 80 years. The class with a moderate blood pressure only had an increased risk of stroke, but not death, compared with the class with a low blood pressure at midlife and a gradual increase.

The trajectories that we identified extend results from prior studies of blood pressure trajectories in young- to middle-aged people. Those studies identified 4 to 5 parallel trajectories in which trajectories with long-term higher blood pressure related to more cardiovascular pathology. In our older population, we also observed that the class with a high midlife blood pressure had the highest risk of stroke and death compared with the class with the lowest blood pressure. However, a novel finding of our study is that the slope of increase was associated with an increasing risk of stroke and competing causes of death. Namely, we identified 2 classes characterized by equally low baseline blood pressure and increasing trajectories, but only the class characterized by steep increases had a high risk of stroke and death. Of note, the risks in that class were even similar to the class with a high midlife blood pressure.

The trajectories and risk patterns identified in this article could inform future research on the cause and potentially treatment guidelines, but the current study does not itself address such pathogenic or treatment questions. Latent class mixture modeling is a useful data-reduction tool and is particularly helpful to describe prototypical and common patterns. It does not, however, account for time-dependent confounding or selection biases that may explain the trajectories and risks estimated. Therefore, the associations with stroke risk seen across our 4 trajectories could be, in part or whole, because of many noncausal explanations, including differences in health behaviors, healthcare utilization, and competing risks throughout the study period. Moreover, findings from the classes are not necessarily applicable to individual participants’ blood pressure effects, particularly because class membership is probabilistic. On the contrary, identifying the patterns described in our study is an important step because they evoke new causal and treatment questions that can motivate future studies to explore the pathogenic significance and predictive value of the associations. Questions raised by the patterns in our study are would we reduce stroke risk if we recommended blood pressure medication to nonhypertensive middle-aged to older patients with fast increases in blood pressure? Or, would we reduce stroke risk if the current treatment level of 140/90 mm Hg or 150/90 mm Hg is lowered to also include people with moderately elevated blood pressure? In addition, trajectories may inform physicians about people who need further attention for their high risk of stroke or death.

Combining our study results with previous evidence, we can speculate to the biological plausibility that treating middle-aged to older patients with (1) moderate blood pressure or (2) fast increasing blood pressure could reduce strokes. The first is supported by previous studies that found a relationship between prehypertension and stroke, and less of prehypertension with other vascular disease. This suggests that the brain may be particular vulnerable to vascular damage. Whether it is likely that treatment of fast increasing blood pressure reduces stroke and death is less clear. It is known that vascular stiffness increases with aging. This leads to an increase in blood pressure and may explain the gradually increasing blood pressure trajectory in the largest part of the population. However, this does not explain why another class was characterized by a much steeper increase. It may be that this trajectory reflects a higher vascular age. This is supported by our findings that associations with stroke attenuated after adjusting for other cardiovascular risk factors. They may have stiffer vessels, which could lead to a steeper increase or a blood pressure resistant to treatment. The higher vascular age may then contribute to the increased risk of stroke and death. Furthermore, the steep increase in blood pressure may trigger rupture of an arteriole leading to a hemorrhagic stroke. Knowing whether a fast increasing blood pressure causally relates to stroke and death is important, because people with fast increasing blood pressure may be missed using current guidelines, leading to undertreatment. Correspondingly, only 33% of the people in the fast increasing class used blood pressure–lowering medication at their end of follow-up. On
the contrary, this could also mean that this class reflects people with more unhealthy behavior that are less adherent to medication themselves. Further research is necessary to unravel the pathogenic background of the trajectories. This should include the question whether some trajectories reflect advancing stages of vascular ageing. For example, with advancing vascular age, people may move from an increasing trajectory to the trajectory of consistently high blood pressure.

Strengths of our study are the large study population, the use of repeated measures of blood pressure over a long follow-up, and the thorough collection of stroke assessments. However, our study also has some limitations. We only examined associations with all stroke, numbers were too small to examine stroke subtypes. Furthermore, we obtained a maximum of only 5 measurements of blood pressure per patient. More measurements would probably lead to more precise results and possibly more or differently defined trajectories. It might also reduce the effect of regression to the mean and within-individual variability. Moreover, there may have been misclassification among classes because of individual variability or reliability in blood pressure assessments. Nevertheless, the trajectories may aid detection of high-risk patients even if the trajectories are, in part, explained by a white-coat effect or variability. In addition, the trajectories may be less reliable at old ages when we had fewer measurements although our trajectories were consistent up through the age of 80 years whether later assessments were included in the model. Finally, we did not have information about blood pressure at earlier ages. Future studies should examine the lifetime trajectory of blood pressure and the risk of stroke.

Perspectives

Treatment of blood pressure to reduce the risk of stroke is currently focused on blood pressure levels. In this population-based study on blood pressure trajectories, we had the novel finding that the trajectory with fast increasing blood pressure was related to a high risk of stroke and death. It shows that single values of blood pressure do not tell the whole story. This may inspire future studies to examine the predictive value of blood pressure trajectories for stroke and mortality. In addition, future studies are needed to determine the pathogenic significance of blood pressure changes. If the blood pressure slope is causally related to stroke and not just a reflection of an individual’s health behavior, it may be a novel target for prevention.

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Disclosures

None

References

Novelty and Significance

**What Is New?**

- We identified 4 trajectories of systolic blood pressure in people aged ≥55 years and assessed the risk of stroke and death across those trajectories. The class with a normal blood pressure at midlife that gradually increased had the lowest risk of stroke and competing causes of death. The class with high blood pressure at midlife and the class with a normal blood pressure at midlife, but a steep increase, had the highest risk of stroke and competing causes of death. The class with a moderate blood pressure at midlife and throughout had a longer survival, but a higher risk of stroke.

**What Is Relevant?**

- Not only levels of blood pressure but also trajectories of blood pressure over time are associated with the risk of stroke and mortality. Of particular novelty is the class characterized by a steep increase in blood pressure at midlife that gradually increased had the lowest risk of stroke and competing causes of death. The class with high blood pressure at midlife and the class with a normal blood pressure at midlife, but a steep increase, had the highest risk of stroke and competing causes of death. The class with a moderate blood pressure at midlife and throughout had a longer survival, but a higher risk of stroke.

**What Is Relevant?**


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