Relation Between Blood Pressure and Clinical Outcome in Hypertensive Subjects With Previous Stroke

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Background—This study investigated whether a mean blood pressure (BP) of <130/80 mm Hg is associated with further reduction in cardiovascular outcomes in treated hypertensive subjects with previous stroke.

Methods and Results—Subjects from the Korea National Health Insurance Service health examinee cohort diagnosed as having stroke and hypertension from January 1st, 2003 and December 31st, 2006 (N=2320) were grouped according to mean systolic (<130, 130–<140, and ≥140 mm Hg) and diastolic (<80, 80–<90, and ≥90 mm Hg) BP recorded during follow-up health examinations. All-cause and cardiovascular mortality over 11 years were compared. Compared with subjects with a systolic BP of ≥140 mm Hg (N=736), subjects with a systolic BP of 130 to <140 mm Hg (N=793) had a significantly lower risk of all-cause death (hazard ratio [HR], 0.61; 95% confidence interval [CI], 0.47–0.79; P<0.001), cardiovascular mortality (HR, 0.39; 95% CI, 0.25–0.61; P<0.001), and fatal ischemic stroke (HR, 0.25; 95% CI, 0.10–0.63; P=0.003). Systolic BP of <130 mm Hg (N=791) was associated with lower risk of nonfatal hemorrhagic stroke. Subjects with a diastolic BP of 80 to <90 mm Hg (N=1100) had significantly lower risk of all-cause death (HR, 0.60; 95% CI, 0.45–0.80; P<0.001) and cardiovascular mortality (HR, 0.45; 95% CI, 0.30–0.70; P<0.001) than those with a diastolic BP of ≥90 mm Hg (N=342). Diastolic BP of <80 mm Hg (N=878) was associated with reduced risk of nonfatal hemorrhagic stroke and further lowering of all-cause mortality and cardiovascular mortality.

Conclusions—BP of <130/80 mm Hg was associated with improved outcomes in hypertensive subjects with previous stroke. (J Am Heart Assoc. 2017;6:e007102. DOI: 10.1161/JAHA.117.007102.)

Key Words: hypertension • mortality • myocardial infarction • stroke

Recently, the SPRINT (Systolic Blood Pressure Intervention Trial) demonstrated that the treatment goal of systolic blood pressure (SBP) of <120 mm Hg was superior to the SBP goal of <140 mm Hg in reducing cardiovascular risk.1 Although the SPRINT study included subjects with high cardiovascular risk, it excluded hypertensive subjects with previous stroke based on the SPS3 (Secondary Prevention of Small Subcortical Strokes) trial, an open-label randomized study that demonstrated the benefit of strict SBP lowering in subjects with previous lacunar infarction.2 Compared with subjects randomized to a target SBP of 130 to 149 mm Hg, subjects randomized to a lower SBP target of <130 mm Hg demonstrated a nonsignificant reduction in the primary outcome of all strokes and a significantly lower rate of intracerebral hemorrhage.2 Consequently, the American Stroke Association proposes the IIb recommendation for a target SBP of 130 mm Hg in subjects with previous lacunar infarction.3 However, the SPS3 study was limited by its inclusion of only subjects with previous lacunar infarction, relative lack of statistical power, 2-by-2 multifactorial design, and enrollment of both normotensive and hypertensive subjects. Therefore, whether strict SBP lowering is beneficial for all hypertensive subjects with previous stroke is unclear. However, it is difficult to verify this through large-scale clinical studies, so using observational cohort data may be helpful.4

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Accompanying Data S1 and Tables S1 through S12 are available at http://jaha.ahajournals.org/content/6/12/e007102/DC1/embed/inline-supplementary-material-1.pdf

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The present study aimed to evaluate whether lower mean BP in hypertensive subjects with previous stroke has a beneficial effect on reducing cardiovascular events, using the National Health Insurance Service (NHIS) cohort.

Methods

Study Population

This study used the NHIS health examinee cohort, comprising 514,866 individuals randomly selected from the NHIS health examination database in 2002. The NHIS cohort profile was previously reported. The NHIS provides free health examinations to eligible NHIS members aged ≥40 years. Detailed information about the health examination is described in Data S1. The intellectual property right of this database belongs to the National Health Insurance corporation. As such, we are not authorized to open the database to the public. However, any investigator can apply for use of the database because it has been open to the public for research purpose (https://nhiss.nhis.or.kr/). This cohort was followed up for 11 years until 2013. The cohort data consisted of qualifications; medical service claims; pharmacy claims; and health examination findings, including anthropometric data, blood chemistry, urine analysis, chest radiography, and information about lifestyle and personal and familial history of hypertension. The disposition of the study cohort is shown in Figure 1. We selected subjects who had been diagnosed as having stroke (KCD codes I60–I64), requiring hospitalization, and hypertension (KCD codes I10–I13) between January 1, 2003 and December 31, 2006 for inclusion in the study population. The KCD system is based on and similar to the International Classification of Diseases, Tenth Revision (ICD-10). Stroke was classified into hemorrhagic stroke (KCD codes I60–I62), ischemic stroke (KCD code I63), and unspecified stroke (KCD code I64). Subjects diagnosed as having stroke and hypertension either simultaneously or separately during the index period were included; 1337 of the subjects received a diagnosis of hypertension before the diagnosis of stroke. Individuals diagnosed as having a previous or active malignancy (KCD codes C00–C97) after stroke diagnosis were excluded. In addition, individuals with prescription records for antihypertensive medications for <1 year during the follow-up or who had undergone health examination only once between January 1, 2003 and December 31, 2013 were excluded. Ultimately, 2320 individuals were included in the analysis. The Institutional Review Board of Yonsei University Health System approved the study (Institutional Review Board number 4-2016-1043), with waiver of informed consent because this was a retrospective observational study of an anonymized data set.

Definition of Medication History

Information about medications during the follow-up was obtained using a prescription database after the index date. We categorized the 5 first-line antihypertensive agents into 4 classes: renin-angiotensin system blocker; β-blocker; calcium channel blocker; and diuretics, including hydrochlorothiazide, chlortalidone, and metolazone. Subjects who had prescription data for antihypertensive agents for at least 1 year were assumed to be taking the medication. The first prescription date and total prescription duration of each medication were obtained from the prescription database. Only individuals who had taken antihypertensive agents for at least 1 year during follow-up were included. In addition, subjects who had taken aspirin or a statin for at least 1 year were assumed to be taking these medications for secondary stroke prevention. Diabetes mellitus was defined as a diagnosis of diabetes mellitus (KCD codes E11–E14) with prescription data for antidiabetic medications before the diagnosis of stroke. Atrial fibrillation was determined by the presence of the corresponding diagnostic code (KCD code I48).

BP Measurement and Classification

BP was measured in hospitals and clinics certified as medical health examination centers by the Korean National Health Insurance Corporation. The measurement protocol was for brachial BP after 5 minutes of rest in the sitting position. BP measurement was repeated if the first measurement was
BP was measured by qualified medical personnel at each health examination center. Both automatic oscillometric devices and mercury sphygmomanometers were used for BP measurements. The choice of device was left to the discretion of individual examination centers, with the preferred recommendation for a mercury sphygmomanometer until 2015, when the sale of mercury sphygmomanometers was banned.

We defined strict SBP control as mean SBP of <130 mm Hg, consistent with the SPS3 study. Although diastolic BP (DBP) of <90 mm Hg is recommended in the current guidelines, studies using J curves have indicated that cardiovascular risk increases at <60 to 70 mm Hg. Therefore, we also aimed to determine whether DBP lowering at <80 mm Hg was beneficial in poststroke hypertensive subjects.

The mean value of BP at all health examinations during the follow-up was used to determine the BP target that subjects had achieved. The study population was divided into 3 groups according to observed mean SBP and DBP: (1) mean SBP of <130 mm Hg (N=791), 130 to <140 mm Hg (N=793), and ≥140 mm Hg (N=736); and (2) mean DBP of <80 mm Hg (N=878), 80 to <90 mm Hg (N=1100), and ≥90 mm Hg (N=342).

Follow-Up and Outcome Measurement

The mean and median follow-up duration were 2987±757 and 3092 days (interquartile range, 2151–3468 days), respectively. The primary outcomes were all-cause mortality and cardiovascular mortality. The dates and causes of death were obtained from the qualification data in the cohort database, which was prepared by Statistics Korea. Clinical outcomes were assessed after the diagnosis of stroke. Cardiovascular mortality was defined as death from a circulatory system disease (KCD codes I00–I99). Causes of cardiovascular mortality were further categorized as myocardial infarction (MI; KCD codes I21–I23), hemorrhagic stroke (KCD codes I60–I62), and ischemic stroke (KCD code I63). We also analyzed rates of nonfatal MI and nonfatal stroke requiring hospitalization. We defined nonfatal stroke as rehospitalization with either nonfatal hemorrhagic or ischemic stroke as the major diagnosis, according to KCD code.

Statistical Analysis

Household income was categorized as upper 20%, middle 40%, and lower 40% based on income levels provided by the NHIS. Residential areas were classified as metropolitan cities or
| Characteristics                  | Observed Mean SBP, mm Hg | <130 (N=791) | 130–<140 (N=793) | ≥140 (N=736) | P Value |
|---------------------------------|---------------------------|-------------|-----------------|-------------|---------|
| Types of stroke                 |                           |             |                 |             |         |
| Hemorrhagic                     |                           | 158 (20.0)  | 139 (17.5)      | 144 (19.6)  | 0.377   |
| Ischemic                        |                           | 606 (76.6)  | 619 (78.1)      | 571 (77.6)  |         |
| Unspecified                     |                           | 27 (3.4)    | 35 (4.4)        | 21 (2.9)    |         |
| SBP, mm Hg                      |                           | 122.7±5.8   | 134.3±2.8       | 149.2±9.0   | <0.001  |
| No. of BP measurements          |                           | 4.6±1.9     | 4.7±1.9         | 3.9±1.8     | <0.001  |
| Age, y                          |                           | 59.1±9.0    | 60.6±9.1        | 62.4±9.1    |         |
| Sex                             |                           | 0.136       |                 |             |         |
| Male                            |                           | 430 (54.4)  | 437 (55.1)      | 435 (59.1)  |         |
| Female                          |                           | 361 (45.6)  | 356 (44.9)      | 301 (40.9)  |         |
| Residential area                |                           | 0.118       |                 |             |         |
| Metropolitan                    |                           | 281 (35.5)  | 243 (30.6)      | 246 (33.4)  |         |
| Province                         |                           | 510 (64.5)  | 550 (69.4)      | 490 (66.6)  |         |
| Household income                |                           | 0.005       |                 |             |         |
| Upper 20%                       |                           | 249 (31.5)  | 208 (26.2)      | 178 (24.2)  |         |
| Middle 40%                      |                           | 309 (39.1)  | 300 (37.8)      | 294 (39.9)  |         |
| Lower 40%                       |                           | 233 (29.5)  | 285 (35.9)      | 264 (35.9)  |         |
| Smoking status                  |                           | 0.572       |                 |             |         |
| Never smoker                    |                           | 517 (65.4)  | 546 (68.9)      | 504 (68.5)  |         |
| Ex-smoker                       |                           | 62 (7.8)    | 57 (7.2)        | 57 (7.7)    |         |
| Current smoker                  |                           | 212 (26.8)  | 190 (24.0)      | 175 (23.8)  |         |
| Alcohol frequency               |                           | 0.133       |                 |             |         |
| Never                           |                           | 492 (62.2)  | 500 (63.1)      | 447 (60.7)  |         |
| 2–3 Drinks/mo                   |                           | 96 (12.1)   | 79 (10.0)       | 68 (8.2)    |         |
| 1–2 Drinks/wk                   |                           | 93 (11.8)   | 86 (10.8)       | 94 (12.8)   |         |
| 3–4 Drinks/wk                   |                           | 64 (8.1)    | 59 (7.4)        | 57 (7.7)    |         |
| Daily                           |                           | 46 (5.8)    | 69 (8.7)        | 70 (9.5)    |         |
| Body mass index, kg/m$^2$       |                           | 24.3±2.9    | 24.4±3.0        | 24.4±3.1    | 0.781   |
| Total cholesterol, mg/dL        |                           | 206.6±44.4  | 206.5±43.2      | 204.3±42.1  | 0.530   |
| Fasting glucose, mg/dL          |                           | 106.4±53.0  | 104.1±35.6      | 114.2±62.8  | <0.001  |
| Baseline SBP, mm Hg             |                           | 127.8±14.3  | 139.0±15.2      | 155.5±19.0  | <0.001  |
| Baseline DBP, mm Hg             |                           | 80.0±10.3   | 85.1±11.2       | 92.1±12.8   | <0.001  |
| History of DM                   |                           | 46 (5.8)    | 47 (5.9)        | 51 (6.9)    | 0.614   |
| History of atrial fibrillation  |                           | 31 (3.9)    | 19 (2.4)        | 8 (1.1)     | 0.002   |
| Medications during follow-up    |                           |             |                 |             |         |
| RASBs                           |                           | 536 (67.8)  | 566 (71.4)      | 519 (70.5)  | 0.263   |
| RASB duration, d                |                           | 1580.5±1201.7| 1618.9±1193.0 | 1605.4±1218.3| 0.836   |
| β-Blockers                      |                           | 202 (25.5)  | 221 (27.9)      | 234 (31.8)  | 0.024   |
| β-Blocker duration, d           |                           | 1023.2±1189.8| 901.6±1024.2  | 931.2±1052.8| 0.278   |
| CCBs                            |                           | 540 (68.3)  | 591 (74.5)      | 576 (78.3)  | <0.001  |

Continued
Table 1. Continued

| Characteristics                  | Observed Mean SBP, mm Hg | P Value |
|----------------------------------|--------------------------|---------|
|                                 | <130 (N=791)             | 130–140 (N=793) | ≥140 (N=736) |
| CCB duration, d                 | 1668.7±1266.7            | 1749.2±1224.0 | 1782.9±1288.5 | 0.227 |
| Diuretics                       | 171 (21.6)               | 240 (30.3)    | 212 (28.8)    | <0.001 |
| Diuretic duration, d            | 782.6±896.9              | 863.1±909.3   | 779.0±869.7   | 0.325 |
| Statins                         | 362 (45.8)               | 340 (42.9)    | 297 (40.4)    | 0.102 |
| Statin duration, d              | 1351.4±1086.1            | 1210.4±1028.0 | 1274.0±1076.0 | 0.068 |
| Aspirin                         | 368 (46.5)               | 340 (42.9)    | 322 (43.8)    | 0.314 |
| Aspirin duration, d             | 1068.4±852.2             | 1012.4±858.0  | 953.7±911.1   | 0.151 |
| Warfarin                        | 55 (7.0)                 | 36 (4.5)      | 27 (3.7)      | 0.010 |
| Warfarin duration, d            | 1454.3±1455.9            | 1100.1±1213.7 | 910.3±1175.6  | 0.045 |
| P2Y12 duration, d               | 284 (35.9)               | 272 (34.3)    | 265 (36.0)    | 0.732 |
| P2Y12                            | 1344.1±1144.5            | 1377.1±1144.9 | 1267.9±1090.3 | 0.385 |
| Follow-up duration, d           | 3087.6±669.4             | 3030.2±663.4  | 2832.6±904.0  | <0.001 |

Data are presented as mean±SD or number (percentage). Each type of stroke was defined with diagnostic codes, as follows: hemorrhagic stroke, I60 to I62; ischemic stroke, I63; and unspecified stroke, I64. BP indicates blood pressure; CCB, calcium channel blocker; DBP, diastolic BP; DM, diabetes mellitus; RASB, renin-angiotensin system blocker; and SBP, systolic BP.

provinces. Group differences in continuous variables were analyzed by using 1-way analysis of variance. Categorical variables were summarized as numbers and percentages of the total group and compared by χ² test. The effects of BP on all-cause mortality and cardiovascular mortality were analyzed by using Kaplan-Meier curves. The association between BP and clinical events, including both fatal and nonfatal outcomes, was evaluated by using Cox proportional hazard models with the covariate adjustment method using the propensity scores, because some end points had a rare event problem when we used the multivariate Cox proportional hazard model with all confounders. The effect of each level of BP on mortality and clinical events was determined by comparison to the uncon- trolled hypertension group (SBP ≥140 mm Hg or DBP ≥90 mm Hg). We also compared the effect of each BP level on mortality and clinical events by comparison to the SBP of 130 to <140 mm Hg and DBP of 80 to <90 mm Hg groups. Propensity scores were assigned using multinomial logistic regression for groups stratified by mean SBP and DBP based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline SBP, baseline DBP, diabetes mellitus history, and atrial fibrillation history. Medication exposure was not included to estimate propensity score because it is information of medication after the index date. Instead, a subgroup analysis was conducted for aspirin or statin users (Tables S1 and S2) and subjects without baseline atrial fibrillation (Tables S3 and S4). In addition, we analyzed the subject regardless of duration of antihypertensive medication (Tables S5 and S6).

All statistical analyses were performed using R statistical software, version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria). All tests were 2 sided, and statistical significance was defined as P<0.05.

Results

Demographic Data

Clinical characteristics of the study population, according to mean SBP and DBP grouping, are shown in Tables 1 and 2. The proportions of ischemic stroke and hemorrhagic stroke were 77.4% and 19.8%, respectively. Previous stroke type did not differ according to mean SBP group. The SBP of <130 mm Hg group included a higher percentage of subjects with atrial fibrillation and a significantly lower proportion of subjects taking β-blockers, calcium channel blockers, and diuretics. Although the percentage of subjects taking aspirin and statins during the follow-up did not significantly differ, there was a higher percentage of warfarin users among subjects with an SBP of <130 mm Hg.

Unlike mean SBP, subjects with a higher mean DBP had a higher percentage with hemorrhagic stroke. The group with a mean DBP of <80 mm Hg had a significantly lower percentage of subjects taking calcium channel blockers and diuretics and a significantly higher percentage of subjects taking aspirin, statins, and warfarin.

Clinical Outcomes According to Mean SBP and DBP

Kaplan-Meier analyses for all-cause death and cardiovascular death, according to mean SBP and DBP, revealed significantly
Table 2. Clinical Characteristics of the Total Study Population According to Observed Mean DBP (N=2320)

| Characteristics                  | Observed Mean DBP, mm Hg | Observed Mean DBP, mm Hg | Observed Mean DBP, mm Hg | P Value |
|----------------------------------|---------------------------|---------------------------|---------------------------|---------|
|                                  | <80 (N=878)               | 80–<90 (N=1100)           | ≥90 (N=342)               |         |
| Types of stroke                  |                           |                           |                           | 0.008   |
| Hemorrhagic                      | 148 (16.9)                | 209 (19.0)                | 84 (24.6)                 |         |
| Ischemic                         | 693 (78.9)                | 850 (77.3)                | 253 (74.0)                |         |
| Unspecified                      | 37 (4.2)                  | 41 (3.7)                  | 5 (1.5)                   |         |
| DBP, mm Hg                       | 74.9±3.9                  | 83.9±2.6                  | 94.5±5.4                  | <0.001  |
| No. of BP measurements           | 4.5±1.7                   | 4.6±2.0                   | 3.7±2.0                   | <0.001  |
| Age, y                           | 61.2±8.6                  | 60.6±9.3                  | 59.4±9.9                  | 0.008   |
| Sex                              |                           |                           |                           | 0.001   |
| Male                             | 450 (51.3)                | 645 (58.6)                | 207 (60.5)                |         |
| Female                           | 428 (48.7)                | 455 (41.4)                | 135 (39.5)                |         |
| Residential area                 |                           |                           |                           | 0.498   |
| Metropolitan                     | 299 (34.1)                | 352 (32.0)                | 119 (34.8)                |         |
| Province                          | 579 (65.9)                | 748 (68.0)                | 223 (65.2)                |         |
| Household income                 |                           |                           |                           | 0.095   |
| Upper 20%                        | 264 (30.1)                | 287 (26.1)                | 84 (24.6)                 |         |
| Middle 40%                       | 335 (38.2)                | 441 (40.1)                | 127 (37.1)                |         |
| Lower 40%                        | 279 (31.8)                | 372 (33.8)                | 131 (38.3)                |         |
| Smoking status                   |                           |                           |                           | 0.561   |
| Never smoker                     | 608 (69.2)                | 739 (67.2)                | 220 (64.3)                |         |
| Ex-smoker                        | 61 (6.9)                  | 86 (7.8)                  | 29 (8.5)                  |         |
| Current smoker                   | 209 (23.8)                | 275 (25.0)                | 93 (27.2)                 |         |
| Alcohol frequency                |                           |                           |                           | <0.001  |
| Never                            | 589 (67.1)                | 671 (61.0)                | 179 (52.3)                |         |
| 2–3 Drinks/mo                    | 94 (10.7)                 | 113 (10.3)                | 36 (10.5)                 |         |
| 1–2 Drinks/wk                    | 86 (9.8)                  | 132 (12.0)                | 55 (16.1)                 |         |
| 3–4 Drinks/wk                    | 52 (5.9)                  | 89 (8.1)                  | 39 (11.4)                 |         |
| Daily                            | 57 (6.5)                  | 95 (8.6)                  | 33 (9.6)                  |         |
| Body mass index, kg/m²           | 24.2±2.9                  | 24.4±3.0                  | 24.8±3.1                  | 0.009   |
| Total cholesterol, mg/dL         | 206.9±46.2                | 205.2±41.5                | 204.9±41.1                | 0.638   |
| Fasting glucose, mg/dL           | 109.2±54.0                | 107.0±46.4                | 108.9±60.4                | 0.609   |
| Baseline SBP, mm Hg              | 131.6±16.7                | 142.1±17.6                | 157.9±20.6                | <0.001  |
| Baseline DBP, mm Hg              | 78.0±9.3                  | 87.4±10.0                 | 98.9±13.0                 | <0.001  |
| History of DM                    | 60 (6.8)                  | 63 (5.7)                  | 21 (6.1)                  | 0.598   |
| History of atrial fibrillation   | 30 (3.4)                  | 20 (1.8)                  | 8 (2.3)                   | 0.076   |
| Medications during follow-up     |                           |                           |                           |         |
| RASBs                            | 607 (69.1)                | 768 (69.8)                | 246 (71.9)                | 0.632   |
| RASB duration, d                 | 1585.7±1195.8             | 1621.1±1217.2             | 1580.7±1182.2             | 0.785   |
| β-Blockers                       | 244 (27.8)                | 293 (26.6)                | 120 (35.1)                | 0.009   |
| β-Blocker duration, d            | 1006.3±1115.8             | 901.4±1077.0              | 957.9±1051.3              | 0.322   |
| CCBs                             | 603 (68.7)                | 848 (77.1)                | 256 (74.9)                | <0.001  |

Continued
Table 2. Continued

| Characteristics       | Observed Mean DBP, mm Hg | P Value |
|-----------------------|--------------------------|---------|
|                       | <80 (N=678)              | 80–<90 (N=1100) | ≥90 (N=342) |
| CCB duration, d       | 1634.9±1263.6            | 1820.0±1246.5 | 1702.4±1276.6 | 0.008 |
| Diuretics             | 209 (23.8)               | 312 (28.4)    | 102 (29.8)    | 0.031 |
| Diuretic duration, d  | 839.7±920.5              | 796.9±883.0   | 790.3±863.3   | 0.727 |
| Statins               | 424 (48.3)               | 452 (41.1)    | 123 (36.0)    | <0.001 |
| Statin duration, d    | 1420.5±1080.6            | 1227.1±1034.5 | 1263.5±1091.8 | 0.006 |
| Aspirin               | 432 (49.2)               | 466 (42.4)    | 132 (38.6)    | 0.001 |
| Aspirin duration, d   | 1115.4±990.5             | 966.3±910.7   | 874.4±873.9   | 0.001 |
| Warfarin              | 58 (6.6)                 | 43 (3.9)      | 17 (5.0)      | 0.025 |
| Warfarin duration, d  | 1376.6±1428.5            | 1099.4±1215.2 | 939.8±1252.0  | 0.184 |
| P2Y12                 | 322 (36.7)               | 385 (35.0)    | 114 (33.3)    | 0.512 |
| P2Y12 duration, d     | 1334.0±1150.2            | 1359.4±1119.2 | 1223.8±1090.3 | 0.391 |
| Follow-up duration, d | 3084.3±681.6             | 2966.0±737.0  | 2805.0±947.2  | <0.001 |

Data are presented as mean±SD or number (percentage). Each type of stroke was defined with diagnostic codes, as follows: hemorrhagic stroke, I60 to I62; ischemic stroke, I63; and unspecified stroke, I64. BP indicates blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; DM, diabetes mellitus; RASB, renin-angiotensin system blocker; and SBP, systolic blood pressure.

lower cumulative all-cause (SBP, log-rank P<0.001 [Figure 2A]; DBP, P<0.001 [Figure 2B]) and cardiovascular (SBP, log-rank P<0.001 [Figure 2C]; DBP, P<0.001 [Figure 2D]) deaths in lower BP groups compared with the higher BP groups (SBP ≥140 mm Hg and DBP ≥90 mm Hg).

Table 3 shows the results of Cox proportional hazard models for all-cause death, cardiovascular death, detailed cause of death, and nonfatal events, including MI and stroke, according to mean SBP. The propensity-adjusted model revealed that subjects with a mean SBP of 130 to <140 mm Hg had a significantly lower risk of all-cause death (hazard ratio [HR], 0.61; 95% confidence interval [CI], 0.47–0.79; P<0.001), cardiovascular mortality (HR, 0.39; 95% CI, 0.25–0.61; P<0.001), and fatal ischemic stroke (HR, 0.25; 95% CI, 0.10–0.63; P=0.003) compared with subjects with a mean SBP of ≥140 mm Hg. There was no additional benefit for mean SBP of <130 mm Hg with regard to all-cause or cardiovascular death. In terms of nonfatal events, the risks of nonfatal MI and nonfatal ischemic stroke did not differ according to mean SBP groups. However, the risk of nonfatal hemorrhagic stroke was significantly lower in the mean SBP of <130 mm Hg group (HR, 0.57; 95% CI, 0.33–0.97; P=0.038) compared with subjects with a mean SBP of ≥140 mm Hg.

Subjects with a mean DBP of 80 to <90 mm Hg had a significantly lower risk of all-cause death (HR, 0.60; 95% CI, 0.45–0.80; P<0.001) and cardiovascular mortality (HR, 0.45; 95% CI, 0.30–0.70; P<0.001) compared with subjects with a mean DBP of ≥90 mm Hg (Table 4). Mean DBP of <80 mm Hg was associated with a significantly lower risk of all-cause death (HR, 0.45; 95% CI, 0.32–0.63; P<0.001), cardiovascular mortality (HR, 0.29; 95% CI, 0.17–0.49; P<0.001), fatal MI (HR, 0.04; 95% CI, 0.01–0.28; P=0.001), and fatal hemorrhagic stroke (HR, 0.21; 95% CI, 0.05–0.92; P=0.039). Mean DBP of <80 mm Hg was associated with further reduction in all-cause mortality, cardiovascular mortality, and fatal MI compared with subjects with a mean DBP of 80 to <90 mm Hg (Table 4). However, the risk of nonfatal MI was significantly higher in subjects with a mean DBP of <90 mm Hg compared with subjects with a mean DBP of 80 to <90 mm Hg. Subjects with a mean DBP of 80 to <90 mm Hg had a trend for lower risk of nonfatal hemorrhagic stroke (HR, 0.65; 95% CI, 0.40–1.07; P=0.091), whereas subjects with a mean DBP of <80 mm Hg were associated with a significantly lower risk of nonfatal hemorrhagic stroke (HR, 0.47; 95% CI, 0.26–0.85; P=0.012). To exclude the possibility of events being caused by the initial stroke itself, we performed an additional analysis to exclude subjects who died within 1 year from the index stroke event (Tables S7 and S8) and observed a similar trend in clinical outcomes compared with the original analyses. In addition, we analyzed the subject regardless of duration of antihypertensive medication. This also showed similar results (Tables S5 and S6). Further analysis of the effect of mean SBP of <120 mm Hg showed a tendency for lower risk of cardiovascular death and fatal ischemic stroke. The risks of both fatal and nonfatal events were not significantly lower in subjects with a mean SBP of <120 mm Hg compared with subjects with a mean SBP of ≥140 mm Hg (Table S9). Mean DBP of <70 mm Hg showed a tendency for reduced risk of cardiovascular death, but there was no reduction in risk of other outcomes (Table S10). When DBP of 80 to <90 mm Hg was
used as a reference, DBP of 70 to <80 mm Hg had a significantly higher risk of nonfatal MI (Table S10).

Clinical Outcomes According to Mean SBP and DBP in Subjects Taking Aspirin and/or Statins During Follow-Up

The clinical characteristics of study subjects who were taking aspirin or statins are shown in Tables S1 and S2, respectively. Subjects with a mean SBP of 130 to <140 mm Hg had a significantly lower risk of cardiovascular mortality (HR, 0.39; 95% CI, 0.19–0.81; P=0.012; Table 5) than subjects with a mean SBP of >140 mm Hg. In terms of DBP, subjects with a mean DBP of 80 to <90 mm Hg had a significantly lower risk of all-cause death (HR, 0.54; 95% CI, 0.34–0.87; P=0.012), cardiovascular mortality (HR, 0.28; 95% CI, 0.14–0.60; P=0.001), and fatal MI (HR, 0.12; 95% CI, 0.02–0.61; P=0.011) than subjects with a mean DBP of ≥90 mm Hg (Table 6). Mean DBP of <80 mm Hg was associated with a significantly lower risk of all-cause death, cardiovascular

Figure 2. Kaplan-Meier curves for all-cause death according to mean systolic (A) and diastolic (B) blood pressure levels and for cardiovascular death according to mean systolic (C) and diastolic (D) blood pressure levels.

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Table 3. Cox Proportional Hazard Models for Mortality According to Observed Mean SBP Groups in the Total Study Population

| Outcome                  | Category, mm Hg | Unadjusted Age and Sex Adjusted | Propensity Adjusted group: ≥140 | Propensity Adjusted (Reference group: 130–<140) |
|--------------------------|-----------------|--------------------------------|---------------------------------|-----------------------------------------------|
| All-cause death          | <130            | 0.48 (0.38–0.61) <0.001        | 0.65 (0.51–0.82) <0.001        | 0.65 (0.48–0.87) 0.005                      |
|                          | 130–<140        | 0.52 (0.41–0.66) <0.001        | 0.60 (0.48–0.76) <0.001        | 0.61 (0.47–0.79) <0.001                      |
|                          | ≥140            | Reference                      | Reference                      | 1.07 (0.80–1.41) 0.654                      |
| Cardiovascular death     | <130            | 0.46 (0.32–0.66) <0.001        | 0.61 (0.42–0.89) 0.010         | 0.56 (0.35–0.90) 0.017                      |
|                          | 130–<140        | 0.36 (0.24–0.54) <0.001        | 0.42 (0.28–0.63) <0.001        | 0.39 (0.25–0.61) <0.001                      |
|                          | ≥140            | Reference                      | Reference                      | 1.65 (1.27–2.13) <0.001                      |
| Fatal MI                 | <130            | 0.33 (0.10–1.03) 0.056         | 0.46 (0.14–1.45) 0.182         | 0.54 (0.13–2.25) 0.396                      |
|                          | 130–<140        | 0.34 (0.11–1.06) 0.062         | 0.40 (0.13–1.26) 0.117         | 0.42 (0.12–1.47) 0.176                      |
|                          | ≥140            | Reference                      | Reference                      | 1.27 (0.29–5.49) 0.750                      |
| Fatal hemorrhagic stroke | <130            | 0.20 (0.06–0.68) 0.011         | 0.22 (0.06–0.78) 0.019         | 0.47 (0.11–2.02) 0.312                      |
|                          | 130–<140        | 0.26 (0.09–0.80) 0.018         | 0.28 (0.09–0.85) 0.025         | 0.38 (0.12–1.25) 0.111                      |
|                          | ≥140            | Reference                      | Reference                      | 2.62 (1.80–8.57) 0.111                      |
| Fatal ischemic stroke    | <130            | 0.30 (0.13–0.71) 0.006         | 0.41 (0.17–0.97) 0.044         | 0.23 (0.08–0.66) 0.006                      |
|                          | 130–<140        | 0.30 (0.13–0.72) 0.006         | 0.36 (0.15–0.84) 0.019         | 0.25 (0.10–0.63) 0.003                      |
|                          | ≥140            | Reference                      | Reference                      | 0.92 (0.31–2.77) 0.886                      |
| Nonfatal MI              | <130            | 1.20 (0.64–2.25) 0.579         | 1.35 (0.71–2.57) 0.354         | 1.98 (0.87–4.52) 0.103                      |
|                          | 130–<140        | 0.87 (0.44–1.73) 0.696         | 0.94 (0.47–1.87) 0.864         | 1.19 (0.55–2.55) 0.662                      |
|                          | ≥140            | Reference                      | Reference                      | 0.84 (0.39–1.81) 0.662                      |
| Nonfatal hemorrhagic stroke | <130        | 0.59 (0.39–0.90) 0.015         | 0.56 (0.36–0.86) 0.008         | 0.57 (0.33–0.97) 0.038                      |
|                          | 130–<140        | 0.76 (0.51–1.13) 0.182         | 0.74 (0.50–1.10) 0.134         | 0.76 (0.49–1.18) 0.222                      |
|                          | ≥140            | Reference                      | Reference                      | 1.32 (0.85–2.05) 0.222                      |
| Nonfatal ischemic stroke | <130            | 0.85 (0.69–1.05) 0.134         | 0.93 (0.76–1.16) 0.532         | 0.91 (0.70–1.19) 0.494                      |
|                          | 130–<140        | 0.88 (0.71–1.08) 0.232         | 0.93 (0.75–1.15) 0.496         | 0.92 (0.73–1.16) 0.479                      |
|                          | ≥140            | Reference                      | Reference                      | 1.09 (0.86–1.37) 0.479                      |

Propensity-adjusted models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline SBP, baseline diastolic blood pressure, history of diabetes mellitus, and history of atrial fibrillation. CI indicates confidence interval; HR, hazard ratio; MI, myocardial infarction; and SBP, systolic blood pressure.
Table 4. Cox Proportional Hazard Models for Mortality According to Observed Mean DBP Groups in the Total Study Population

| Outcome                  | Category, mm Hg | No. (%) of Events | Unadjusted Age and Sex Adjusted | Propensity Adjusted (Reference group: ≥90) | Propensity Adjusted (Reference group: 80–90) |
|--------------------------|-----------------|-------------------|--------------------------------|--------------------------------------------|--------------------------------------------|
|                          |                 |                   | HR (95% CI) | P Value | HR (95% CI) | P Value | HR (95% CI) | P Value | HR (95% CI) | P Value |
| All-cause death          | <80             | 128 (14.58)       | 0.52 (0.40–0.68) | <0.001  | 0.45 (0.34–0.59) | <0.001  | 0.45 (0.32–0.63) | <0.001  | 0.75 (0.58–0.96) | 0.023  |
|                          | 80–<90          | 191 (17.36)       | 0.65 (0.51–0.84) | 0.001   | 0.57 (0.44–0.73) | <0.001  | 0.60 (0.45–0.80) | <0.001  | Reference | Reference |
|                          | ≥90             | 86 (25.15)        | Reference | Reference | Reference | Reference | Reference | Reference | 1.67 (1.25–2.11) | <0.001  |
| Cardiovascular death     | <80             | 43 (4.90)         | 0.37 (0.24–0.57) | <0.001  | 0.33 (0.22–0.51) | <0.001  | 0.29 (0.17–0.49) | <0.001  | 0.63 (0.42–0.96) | 0.031  |
|                          | 80–<90          | 71 (6.45)         | 0.51 (0.35–0.75) | 0.001   | 0.46 (0.31–0.67) | <0.001  | 0.45 (0.30–0.70) | <0.001  | Reference | Reference |
|                          | ≥90             | 42 (12.28)        | Reference | Reference | Reference | Reference | Reference | Reference | 2.20 (1.44–3.38) | <0.001  |
| Fatal MI                 | <80             | 2 (0.23)          | 0.11 (0.02–0.51) | 0.005   | 0.10 (0.02–0.46) | 0.004   | 0.04 (0.01–0.28) | 0.001   | 0.14 (0.02–0.69) | 0.016  |
|                          | 80–<90          | 10 (0.91)         | 0.44 (0.17–1.16) | 0.095   | 0.39 (0.15–1.02) | 0.055   | 0.32 (0.10–0.97) | 0.044   | Reference | Reference |
|                          | ≥90             | 7 (2.05)          | Reference | Reference | Reference | Reference | Reference | Reference | 3.16 (1.03–9.66) | 0.044  |
| Fatal hemorrhagic stroke | <80             | 4 (0.46)          | 0.19 (0.06–0.64) | 0.007   | 0.18 (0.05–0.60) | 0.005   | 0.21 (0.05–0.92) | 0.039   | 0.55 (0.15–2.01) | 0.368  |
|                          | 80–<90          | 9 (0.82)          | 0.35 (0.13–0.91) | 0.031   | 0.33 (0.13–0.87) | 0.024   | 0.37 (0.13–1.09) | 0.071   | Reference | Reference |
|                          | ≥90             | 8 (2.34)          | Reference | Reference | Reference | Reference | Reference | Reference | 2.70 (0.92–7.91) | 0.071  |
| Fatal ischemic stroke    | <80             | 9 (1.03)          | 0.34 (0.14–0.83) | 0.018   | 0.30 (0.12–0.75) | 0.009   | 0.20 (0.06–0.60) | 0.004   | 0.54 (0.22–1.32) | 0.175  |
|                          | 80–<90          | 16 (1.45)         | 0.49 (0.22–1.08) | 0.077   | 0.44 (0.20–0.98) | 0.045   | 0.37 (0.15–0.88) | 0.025   | Reference | Reference |
|                          | ≥90             | 10 (2.92)         | Reference | Reference | Reference | Reference | Reference | Reference | 2.73 (1.13–6.57) | 0.025  |
| Nonfatal MI              | <80             | 27 (3.08)         | 1.04 (0.50–2.14) | 0.923   | 1.05 (0.51–2.17) | 0.896   | 1.38 (0.56–3.41) | 0.479   | 2.36 (1.23–4.54) | 0.010  |
|                          | 80–<90          | 18 (1.64)         | 0.55 (0.26–1.20) | 0.133   | 0.54 (0.25–1.17) | 0.119   | 0.59 (0.25–1.36) | 0.214   | Reference | Reference |
|                          | ≥90             | 10 (2.92)         | Reference | Reference | Reference | Reference | Reference | Reference | 1.71 (0.73–3.97) | 0.214  |
| Nonfatal hemorrhagic stroke | <80          | 40 (4.56)         | 0.50 (0.31–0.81) | 0.004   | 0.50 (0.31–0.80) | 0.004   | 0.47 (0.26–0.85) | 0.012   | 0.71 (0.46–1.10) | 0.128  |
|                          | 80–<90          | 64 (5.82)         | 0.65 (0.42–1.01) | 0.054   | 0.66 (0.42–1.01) | 0.057   | 0.65 (0.40–1.07) | 0.091   | Reference | Reference |
|                          | ≥90             | 30 (8.77)         | Reference | Reference | Reference | Reference | Reference | Reference | 1.53 (0.94–2.49) | 0.091  |
| Nonfatal ischemic stroke | <80             | 193 (21.98)       | 0.82 (0.64–1.05) | 0.122   | 0.78 (0.61–1.01) | 0.056   | 0.76 (0.56–1.04) | 0.084   | 0.97 (0.79–1.19) | 0.757  |
|                          | 80–<90          | 243 (22.09)       | 0.84 (0.66–1.07) | 0.157   | 0.81 (0.64–1.04) | 0.095   | 0.79 (0.60–1.03) | 0.082   | Reference | Reference |
|                          | ≥90             | 87 (25.44)        | Reference | Reference | Reference | Reference | Reference | Reference | 1.27 (0.97–1.66) | 0.082  |

Propensity-adjusted models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline DBP, history of diabetes mellitus, and history atrial fibrillation. CI indicates confidence interval; DBP, diastolic blood pressure; HR, hazard ratio; and MI, myocardial infarction.
mortality, and fatal MI (Table 6). Mean DBP of <80 mm Hg was associated with a tendency for further reduction in fatal MI compared with subjects with a mean DBP of 80 to <90 mm Hg. However, the risk of nonfatal MI was increased in subjects with a mean DBP of <80 mm Hg compared with subjects with a mean DBP of 80 to <90 mm Hg.

### Table 5. Propensity-Adjusted Cox Proportional Hazard Models for Mortality According to Observed Mean SBP Groups in Aspirin and/or Statin Users

| Mortality                     | Reference group (≥140) | Reference group (130–<140) |
|-------------------------------|------------------------|----------------------------|
|                               | HR (95% CI)            | P Value                    | HR (95% CI)            | P Value                    |
| All-cause death, mm Hg        |                        |                           |                           |                           |
| <130                          | 0.97 (0.61–1.53)       | 0.883                      | 1.41 (0.92–2.17)         | 0.118                      |
| 130–<140                      | 0.69 (0.45–1.04)       | 0.077                      | Reference                | Reference                |
| ≥140                          | Reference              | Reference                  | 1.46 (0.96–2.22)         | 0.077                      |
| Cardiovascular death, mm Hg   |                        |                           |                           |                           |
| <130                          | 0.60 (0.28–1.27)       | 0.180                      | 1.53 (0.71–3.29)         | 0.274                      |
| 130–<140                      | 0.39 (0.19–0.81)       | 0.012                      | Reference                | Reference                |
| ≥140                          | Reference              | Reference                  | 2.57 (1.23–5.38)         | 0.012                      |
| Fatal MI, mm Hg               |                        |                           |                           |                           |
| <130                          | 1.15 (0.18–7.53)       | 0.881                      | 1.99 (0.30–13.10)        | 0.473                      |
| 130–<140                      | 0.58 (0.09–3.60)       | 0.558                      | Reference                | Reference                |
| ≥140                          | Reference              | Reference                  | 1.73 (0.28–10.74)        | 0.558                      |
| Fatal hemorrhagic stroke, mm Hg|                        |                           |                           |                           |
| <130                          | 0.49 (0.03–8.45)       | 0.627                      | 1.22 (0.07–22.76)        | 0.892                      |
| 130–<140                      | 0.40 (0.03–4.76)       | 0.472                      | Reference                | Reference                |
| ≥140                          | Reference              | Reference                  | 2.47 (0.21–29.16)        | 0.472                      |
| Fatal ischemic stroke, mm Hg  |                        |                           |                           |                           |
| <130                          | 0.71 (0.14–3.78)       | 0.692                      | 2.03 (0.35–11.82)        | 0.431                      |
| 130–<140                      | 0.35 (0.06–2.10)       | 0.251                      | Reference                | Reference                |
| ≥140                          | Reference              | Reference                  | 2.84 (0.48–16.96)        | 0.251                      |
| Nonfatal MI, mm Hg            |                        |                           |                           |                           |
| <130                          | 1.69 (0.70–4.04)       | 0.243                      | 1.87 (0.88–4.00)         | 0.105                      |
| 130–<140                      | 0.90 (0.38–2.11)       | 0.809                      | Reference                | Reference                |
| ≥140                          | Reference              | Reference                  | 1.11 (0.47–2.61)         | 0.809                      |
| Nonfatal hemorrhagic stroke, mm Hg|                        |                           |                           |                           |
| <130                          | 0.60 (0.28–1.29)       | 0.193                      | 0.96 (0.48–1.93)         | 0.907                      |
| 130–<140                      | 0.63 (0.32–1.22)       | 0.171                      | Reference                | Reference                |
| ≥140                          | Reference              | Reference                  | 1.50 (0.82–2.81)         | 0.171                      |
| Nonfatal ischemic stroke, mm Hg|                        |                           |                           |                           |
| <130                          | 0.82 (0.59–1.15)       | 0.253                      | 0.92 (0.70–1.22)         | 0.558                      |
| 130–<140                      | 0.90 (0.67–1.20)       | 0.459                      | Reference                | Reference                |
| ≥140                          | 1.12 (0.83–1.49)       | 0.459                      |                           |                           |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline SBP, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation. CI indicates confidence interval; HR, hazard ratio; MI, myocardial infarction; and SBP, systolic blood pressure.

**Discussion**

The key findings from this study are as follows. First, in hypertensive subjects with previous stroke, an SBP of <140 mm Hg was associated with a significant reduction in all-cause mortality, cardiovascular mortality, and fatal
ischemic stroke. Second, an SBP of <130 mm Hg was associated with a significantly lower risk of nonfatal hemorrhagic stroke compared with subjects with a mean SBP of ≥140 mm Hg. Third, a DBP of <80 mm Hg was associated with a further reduction in all-cause mortality, cardiovascular mortality, and fatal MI compared with subjects with a DBP of 80 to <90 mm Hg. However, there was a significant increase in risk of nonfatal MI. Because the association between BP and stroke incidence is stronger in Asian populations than Western populations, the target BP in Asian subjects may differ from that in other ethnicities.12

The present results differ from the SPS3 study, which demonstrated an insignificant benefit of strict SBP control in reducing the composite outcome of fatal MI or vascular death. This discrepancy may be related to the 3.7-year mean follow-up of the SPS3 study, which may have been insufficient to discern a difference in cardiovascular mortality, and limited enrollment to subjects with previous lacunar infarction. However, the SPS3 study detected a significant 63% reduction in intracerebral hemorrhage, which is consistent with this study, in which mean SBP of <130 mm Hg, compared with subjects with a mean SBP of ≥140 mm Hg, was associated with a significant reduction in nonfatal hemorrhagic stroke. In addition, mean DBP of <80 mm Hg showed notable risk reduction for both fatal and nonfatal hemorrhagic stroke. A previous post-hoc analysis and meta-analysis have supported the benefit of strict BP control in hypertensive subjects with stroke. In a subgroup analysis of the ACCORD BP (Action to Control Cardiovascular Risk in Diabetes Blood Pressure Trial), intensive BP treatment was associated with significant reduction in both total stroke and nonfatal stroke.13 In a meta-regression analysis of 618,815 participants in 123 studies, every 10–mm Hg reduction in SBP was associated with a 27% reduction in stroke risk, regardless of baseline disease history, suggesting a significant benefit of strict BP lowering.14 In the VALUE (Valsartan Antihypertensive Long-Term Use Evaluation) study post-hoc analysis, reduction of on-treatment SBP to <130 mm Hg was only beneficial for further reduction of stroke risk, without any benefit for cardiovascular mortality, MI, or congestive heart failure.15

However, some studies have demonstrated a potential for harm with lower BP. In a community-based study of participants from the National Health and Nutrition Examination Survey (1998–2004) with a self-reported history of stroke, a baseline SBP <120 mm Hg was associated with higher all-cause mortality and a trend toward higher vascular mortality compared with normal SBP (120–140 mm Hg) and high SBP (>140 mm Hg).16 Our study differs from this previous study in that we analyzed the difference in cardiovascular mortality risk according to mean SBP during follow-up rather than baseline SBP. In addition, our study excluded subjects with concomitant malignancies or subjects who died within 1 year of the diagnosis of stroke. These factors may have reduced the inclusion of subjects in poorer general condition in the present study, in whom lower baseline BP may be associated with higher mortality.17,18 The significant reductions in both fatal ischemic and nonfatal hemorrhagic stroke in our study are supported by the post-hoc analysis of the INVEST (International Verapamil-Trandolapril Study), which demonstrated a J-shaped phenomenon for MI but not for fatal or nonfatal stroke.10,19 Also, in the post-hoc analysis of the ONTARGET (Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial), a J curve was demonstrated at a mean SBP of <130 mm Hg for total and cardiovascular mortality and coronary events, but not for fatal and nonfatal stroke.20 Further analysis of this study did not reveal an increased risk of clinical outcomes in subjects with a mean SBP of <120 mm Hg or a mean DBP of <70 mm Hg compared with subjects with a mean BP of ≥140/90 mm Hg. However, because the number of subjects with a mean SBP of <120 mm Hg (N=199) or a mean DBP of <70 mm Hg (N=92) was small, these results should be interpreted with caution. In a post-hoc analysis of the PROFESS (Prevention Regimen for Effectively Avoiding Second Strokes) study, subjects with a mean SBP between 120 and 140 mm Hg had the lowest risk of recurrent stroke, and subjects with a mean SBP of <120 mm Hg had an increased risk of recurrent stroke.21 Also, when we analyzed for the presence of the J curve with SBP of 130 to <140 mm Hg or DBP of 80 to <90 mm Hg as reference, we found that DBP of <80 mm Hg was associated with increased risk of nonfatal MI. It is uncertain why there was a reduction in fatal MI but an increase in nonfatal MI for subjects with a mean DBP of <80 mm Hg. It may be that subjects who have a lower mean DBP have a lower severity of MI or that the low number of fatal MIs in this analysis was a chance phenomenon. Another explanation may be the limitation of ICD-10–based diagnosis of nonfatal events. In a study to determine the accuracy of acute MI based on ICD codes using the Korean National Medical Health Insurance claims data, the accuracy of acute MI was 73.1%, according to the European Society of Cardiology/American College of Cardiology criteria.22

Several limitations of this study should be discussed. First, because this study was based on a retrospective cohort analysis, the results can only be interpreted as hypothesis generating. However, this study demonstrated that lower mean BP is associated with a reduction in mortality, cardiovascular mortality, and nonfatal strokes in hypertensive subjects with previous stroke and provides important insight into the potential benefit of strict BP lowering in this population. The ongoing SHOT (Systolic Hypertension Optimal Treatment Trial), a trial enrolling 7500 subjects >65 years with previous stroke or transient ischemic attack to investigate the relationship between SBP treatment targets and recurrent stroke, will help to validate this important issue in hypertension management.23 Second, because this study was based on claims data using ICD-10 diagnosis codes, it was limited in
terms of determining stroke severity. Therefore, we cannot rule out the confounding effect of stroke severity on the outcomes of these subjects. Third, we cannot conclude whether subjects with a relatively well-controlled mean BP were more compliant with their BP, statin, and aspirin prescriptions. However, a similar trend was demonstrated in the Cox regression analysis for subjects taking aspirin and statins. Fourth, because health examinations supported by the National Health Insurance Corporation were performed in various hospitals and clinics, there was a lack of uniformity of BP measuring devices. Fifth, the study subjects were relatively young and able to receive the nationwide health examination. As such, subjects with stroke with more severe disabilities would more than likely have been omitted from participation.

| Mortality                                        | Reference group (≥90) | Reference group (80–<90) |
|-------------------------------------------------|-----------------------|--------------------------|
| All-cause death, mm Hg                           |                       |                          |
| <80                                             | 64 (10.61)            | 0.49 (0.29–0.85)         |
| 80–<90                                          | 70 (10.29)            | 0.54 (0.34–0.87)         |
| ≥90                                             | 31 (16.06)            | Reference                |
| Cardiovascular death, mm Hg                      |                       |                          |
| <80                                             | 20 (3.32)             | 0.18 (0.07–0.42)         |
| 80–<90                                          | 24 (3.53)             | 0.28 (0.14–0.60)         |
| ≥90                                             | 14 (7.25)             | Reference                |
| Fatal MI, mm Hg                                 |                       |                          |
| <80                                             | 1 (0.17)              | 0.01 (0.00–0.19)         |
| 80–<90                                          | 4 (0.59)              | 0.12 (0.02–0.61)         |
| ≥90                                             | 4 (2.07)              | Reference                |
| Fatal hemorrhagic stroke, mm Hg                  |                       |                          |
| <80                                             | 1 (0.17)              | 0.34 (0.01–10.57)        |
| 80–<90                                          | 3 (0.44)              | 0.98 (0.07–13.60)        |
| ≥90                                             | 1 (0.52)              | Reference                |
| Fatal ischemic stroke, mm Hg                     |                       |                          |
| <80                                             | 6 (1.00)              | 0.43 (0.04–4.93)         |
| 80–<90                                          | 3 (0.44)              | 0.33 (0.03–3.58)         |
| ≥90                                             | 1 (0.52)              | Reference                |
| Nonfatal MI, mm Hg                              |                       |                          |
| <80                                             | 24 (3.98)             | 0.93 (0.34–2.52)         |
| 80–<90                                          | 14 (2.06)             | 0.43 (0.17–1.12)         |
| ≥90                                             | 8 (4.15)              | Reference                |
| Nonfatal hemorrhagic stroke, mm Hg               |                       |                          |
| <80                                             | 22 (3.65)             | 0.50 (0.21–1.18)         |
| 80–<90                                          | 25 (3.68)             | 0.50 (0.24–1.04)         |
| ≥90                                             | 15 (7.77)             | Reference                |
| Nonfatal ischemic stroke, mm Hg                  |                       |                          |
| <80                                             | 141 (23.38)           | 0.76 (0.51–1.14)         |
| 80–<90                                          | 152 (22.35)           | 0.79 (0.55–1.13)         |
| ≥90                                             | 48 (24.87)            | Reference                |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline DBP, history of diabetes mellitus, and history atrial fibrillation. CI indicates confidence interval; DBP, diastolic blood pressure; HR, hazard ratio; and MI, myocardial infarction.
Therefore, the results from this study cannot be generalized to the entire stroke population. Sixth, because the inclusion criteria allowed for subjects who received diagnoses of stroke and hypertension either simultaneously or separately during the index period, 1337 were diagnosed as having hypertension before being diagnosed as having stroke. As such, the mean BP reflects the mean BP of the study population from the start of the index period rather than after the stroke event. Because health examinations are performed every 2 years for office workers and annually for manual laborers, a cardiovascular event within 1 year after stroke will most likely reflect the average BP measured during the index period before the development of stroke. We cannot rule out the possibility that BP measured before stroke does not accurately reflect BP after stroke because of more active intervention to lower BP after the stroke event. In addition, the frequency of health examination received varied among the study subjects. However, analyses using the last BP measurement before mortality, clinical events, or the last health examination showed a trend to the original results (Tables S11 and S12).

Seventh, ≈40% of all the subjects with stroke during the index period had a diagnosis of hypertension. Because the diagnosis of hypertension was based on the ICD-10 code of claims data and not on the BP level or prescription of antihypertensive medications, we cannot rule out the possibility that subjects with stroke who had hypertension were missed because of omission of the diagnostic code for hypertension. Because we had aimed to analyze subjects with stroke who had hypertension, we believed that the strict inclusion criteria to analyze only subjects with a diagnosis of hypertension were appropriate. Last, the large difference in the HR for some of the clinical events, such as fatal MI, may be attributable to the relatively few events. Also, because this was a retrospective analysis of an observational cohort, there is a possibility that subjects with a lower BP may have been more compliant with medication and lifestyle modifications, important factors that may have an additive effect on the HR.

In conclusion, in hypertensive subjects with previous stroke, a mean DBP of <80 mm Hg was associated with significant benefit in total mortality, cardiovascular mortality, and some of the nonfatal cardiovascular events. However, there was an increase in nonfatal MI in subjects with a mean DBP of <80 mm Hg compared with subjects with a mean DBP of 80 to <90 mm Hg. Mean SBP of 130 mm Hg was associated with a significantly lower risk of nonfatal hemorrhagic strokes. The results from this study require validation by future randomized clinical trials.

**Perspectives**

Previously, only the SPS3 study sought to demonstrate the potential benefit of strict BP control in patients after stroke. However, because the SPS3 study was performed in patients after lacunar infarction, the benefit of strict BP lowering in all hypertensive patients after stroke is not clear. The results from the present study demonstrate the potential benefit of a BP of <130/80 mm Hg in hypertensive subjects with prior stroke. However, the potential risk for increased risk of nonfatal MI in subjects with a mean DBP of <80 mm Hg was observed. Also, because this study is based on an observational cohort, the results from this study are only hypothesis generating. Nevertheless, the results support the necessity for future studies to demonstrate the benefit of strict BP control in all patients with stroke.

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**Disclosures**

None.

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Data S1.

Health examination program provided by the Korean National Health Insurance Corporation

The Korean National Health Insurance Service provides nationwide health examination program to improve the health of citizens and reduce their health care costs through the prevention of cardio-cerebrovascular diseases affected by lifestyle. Nationwide health examination consists of a general and a life-transition health examination.¹ Employee subscriber, its dependents, regional insurance subscriber who is a regional householder, and its family members can receive the general health examination biennially. For non-office workers among employee subscribers, this examination is conducted annually. The life-transition health examination is given to people reaching ages of 40 and 66, who is eligible to receive the general health examination.¹,² The National Health Insurance Service health examinee cohort (NHIS-HealS) was made with data of nationwide health examinations conducted by the NHIS in 2002–13.³
| Table S1. Clinical characteristics of aspirin and/or statin users according to observed mean systolic blood pressure. |
|---------------------------------------------------------------|
|                                                                |
| **Average SBP, mmHg**                                         |
| <130 mmHg (N=520)                                             |
| 130 to <140 mmHg (N=500)                                      |
| ≥140 mmHg (N=456)                                             |
| **P value**                                                   |
| 122.7±5.9                                                     |
| 134.4±2.8                                                     |
| 148.9±8.8                                                     |
| <0.001                                                       |
| 4.7±1.8                                                       |
| 4.8±1.9                                                       |
| 4.1±1.8                                                       |
| <0.001                                                       |
| 58.6±8.5                                                      |
| 60.5±9.1                                                      |
| 61.7±8.7                                                      |
| <0.001                                                       |
| **Number of BP measurement**                                  |
| 4.7±1.8                                                       |
| 4.8±1.9                                                       |
| 4.1±1.8                                                       |
| <0.001                                                       |
| **Sex, N (%)**                                                |
| Male                                                          |
| 285 (54.8)                                                    |
| 271 (54.2)                                                    |
| 262 (57.5)                                                    |
| 0.564                                                        |
| Female                                                        |
| 235 (45.2)                                                    |
| 229 (45.8)                                                    |
| 194 (42.5)                                                    |
| 0.564                                                        |
| **Residential area, N (%)**                                   |
| Metropolitan                                                  |
| 174 (33.5)                                                    |
| 162 (32.4)                                                    |
| 164 (36.0)                                                    |
| 0.493                                                        |
| Province                                                      |
| 346 (66.5)                                                    |
| 338 (67.6)                                                    |
| 292 (64.0)                                                    |
| 0.493                                                        |
| **Household income, N (%)**                                   |
| Upper 20%                                                     |
| 161 (31.0)                                                    |
| 143 (28.6)                                                    |
| 112 (24.6)                                                    |
| 0.194                                                        |
| Middle 40%                                                    |
| 200 (38.5)                                                    |
| 185 (37.0)                                                    |
| 183 (40.1)                                                    |
| 0.194                                                        |
| Lower 40%                                                     |
| 159 (30.6)                                                    |
| 172 (34.4)                                                    |
| 161 (35.3)                                                    |
| 0.194                                                        |
| **Smoking status, N (%)**                                     |
| Never smoker                                                  |
| 347 (66.7)                                                    |
| 346 (69.2)                                                    |
| 317 (69.5)                                                    |
| 0.862                                                        |
| Ex-smoker                                                     |
| 41 (7.9)                                                      |
| 36 (7.2)                                                      |
| 30 (6.6)                                                      |
| 0.862                                                        |
| Current smoker                                                |
| 132 (25.4)                                                    |
| 118 (23.6)                                                    |
| 109 (23.9)                                                    |
| 0.862                                                        |
| **Alcohol frequency, N (%)**                                  |
| Never                                                         |
| 321 (61.7)                                                    |
| 317 (63.4)                                                    |
| 275 (60.3)                                                    |
| 0.091                                                        |
| 2~3/month                                                    |
| 64 (12.3)                                                      |
| 51 (10.2)                                                     |
| 39 (8.6)                                                      |
| 0.091                                                        |
| 1~2/week                                                     |
| 67 (12.9)                                                      |
| 56 (11.2)                                                      |
| 72 (15.8)                                                     |
| 0.091                                                        |
| 3~4/week                                                     |
| 44 (8.5)                                                      |
| 36 (7.2)                                                      |
| 34 (7.5)                                                      |
| 0.091                                                        |
| Daily                                                        |
| 24 (4.6)                                                      |
| 40 (8.0)                                                      |
| 36 (7.9)                                                      |
| 0.091                                                        |
| **Body mass index, kg/m²**                                    |
| 24.4±2.9                                                     |
| 24.7±2.8                                                     |
| 24.8±3.0                                                     |
| 0.141                                                        |
| **Total cholesterol, mg/dL**                                  |
| 211.2±40.8                                                   |
| 211.8±45.4                                                   |
| 211.1±44.0                                                   |
| 0.960                                                        |
| **Fasting glucose, mg/dL**                                    |
| 107.3±44.0                                                   |
| 106.5±37.7                                                   |
| 113.6±63.9                                                   |
| 0.055                                                        |
| **Baseline SBP, mmHg**                                        |
| 128.0±14.1                                                   |
| 138.8±15.0                                                   |
| 155.6±18.7                                                   |
| <0.001                                                       |
| **Baseline DBP, mmHg**                                        |
| 80.0±10.0                                                    |
| 84.6±11.4                                                    |
| 91.8±12.2                                                    |
| <0.001                                                       |
| **History of DM, N (%)**                                      |
| 30 (5.8)                                                      |
| 31 (6.2)                                                      |
| 31 (6.8)                                                      |
| 0.802                                                        |
| **History of atrial fibrillation, N (%)**                     |
| 19 (3.7)                                                      |
| 12 (2.4)                                                      |
| 5 (1.1)                                                      |
| 0.035                                                        |
| **Antihypertensive medication**                              |
| RASB, N (%)                                                   |
| 379 (72.9)                                                    |
| 398 (79.6)                                                    |
| 358 (78.5)                                                    |
| 0.024                                                        |
| RASB duration, day                                           |
| 1712.3±1220.3                                                 |
| 1828.6±1190.9                                                |
| 1894.0±1204.1                                                |
| 0.073                                                        |
| BB, N (%)                                                    |
| 151 (29.0)                                                    |
| 153 (30.6%)                                                   |
| 156 (34.2)                                                    |
| 0.208                                                        |
| BB duration, day                                             |
| 1116.4±1167.5                                                |
| 978.2±1037.8                                                |
| 1022.1±1110.4                                                |
| 0.353                                                        |
| CCB, N (%)                                                   |
| 358 (68.8)                                                    |
| 384 (76.8)                                                    |
| 375 (82.2)                                                    |
| <0.001                                                        |
| CCB duration, day                                           |
| 1747.7±1283.4                                                |
| 1856.8±1241.7                                                |
| 2014.0±1274.8                                                |
| 0.008                                                        |
| Diuretics, N (%)                                             |
| 118 (22.7)                                                    |
| 174 (34.8)                                                    |
| 158 (34.6)                                                    |
| <0.001                                                        |
| Diuretics duration, day                                      |
| 807.0±864.0                                                  |
| 935.5±938.7                                                  |
| 930.7±934.4                                                  |
| 0.227                                                        |
| Statin, N (%)                                                |
| 362 (69.6)                                                    |
| 340 (68.0)                                                    |
| 297 (65.1)                                                    |
| 0.322                                                        |
| Statin duration, day                                         |
| 1582.6±1015.4                                                |
| 1599.3±1030.4                                                |
| 1436.9±992.7                                                 |
| 0.059                                                        |
|                                | Group 1 | Group 2 | Group 3 | p-value |
|--------------------------------|---------|---------|---------|---------|
| Aspirin, N (%)                 | 368 (70.8) | 340 (68.0) | 322 (70.6) | 0.565   |
| Aspirin duration, day          | 1262.1±931.6 | 1256.2±939.5 | 1224.3±889.7 | 0.825   |
| Follow-up duration, day        | 3161.2±576.5 | 3104.5±532.4 | 3023.8±668.3 | 0.001   |

Data are presented as mean ± SD or N (%).
BB, beta blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; DM, diabetes mellitus; RASB, renin angiotensin system blocker; SBP, systolic blood pressure.
Table S2. Clinical characteristics of aspirin and/or statin users according to observed mean diastolic blood pressure.

|                                | <80 mmHg (N=603) | 80 to <90 mmHg (N=680) | ≥90 mmHg (N=193) | P value |
|--------------------------------|------------------|------------------------|------------------|---------|
| Average DBP, mmHg              | 126.5±8.9        | 137.3±8.3              | 151.8±12.3       | <0.001  |
| Number of BP measurement       | 4.6±1.7          | 4.7±2.0                | 3.9±2.0          | <0.001  |
| Age (year)                     | 60.9±8.4         | 60.1±9.0               | 58.6±9.6         | 0.005   |
| Sex, N (%)                     |                  |                        |                  | 0.008   |
| Male                           | 310 (51.4)       | 385 (56.6)             | 123 (63.7)       |         |
| Female                         | 293 (48.6)       | 295 (43.4)             | 70 (36.3)        |         |
| Residential area, N (%)        |                  |                        |                  | 0.223   |
| Metropolitan                   | 199 (33.0)       | 225 (33.1)             | 76 (39.4)        |         |
| Province                       | 404 (67.0)       | 455 (66.9)             | 117 (60.6)       |         |
| Household income, N (%)        |                  |                        |                  | 0.469   |
| Upper 20%                      | 184 (30.5)       | 184 (27.1)             | 48 (24.9)        |         |
| Middle 40%                     | 227 (37.6)       | 267 (39.3)             | 74 (38.3)        |         |
| Lower 40%                      | 192 (31.8)       | 229 (33.7)             | 71 (36.8)        |         |
| Smoking status, N (%)          |                  |                        |                  | 0.223   |
| Never smoker                   | 430 (71.3)       | 454 (66.8)             | 126 (65.3)       |         |
| Ex-smoker                      | 44 (7.3)         | 51 (7.5)               | 12 (6.2)         |         |
| Current smoker                 | 129 (21.4)       | 175 (25.7)             | 55 (28.5)        |         |
| Alcohol frequency, N (%)       |                  |                        |                  | 0.001   |
| Never                          | 404 (67.0)       | 413 (60.7)             | 96 (49.7)        |         |
| 2–3/month                      | 63 (10.4)        | 70 (10.3)              | 21 (10.9)        |         |
| 1–2/week                       | 67 (11.1)        | 88 (12.9)              | 40 (20.7)        |         |
| 3–4/week                       | 33 (5.5)         | 61 (9.0)               | 20 (10.4)        |         |
| Daily                          | 36 (6.0)         | 48 (7.1)               | 16 (8.3)         |         |
| Body mass index, kg/m²         | 24.3±2.9         | 24.7±2.9               | 25.2±2.8         | <0.001  |
| Total cholesterol, mg/dL       | 211.1±43.5       | 212.0±43.7             | 210.4±41.8       | 0.884   |
| Fasting glucose, mg/dL         | 109.2±43.8       | 108.3±47.7             | 110.4±67.9       | 0.864   |
| Baseline SBP, mmHg             | 131.9±16.5       | 142.4±17.3             | 158.6±21.0       | <0.001  |
| Baseline DBP, mmHg             | 78.2±9.1         | 87.5±10.1              | 99.2±12.4        | <0.001  |
| History of DM, N (%)           | 36 (6.0)         | 43 (6.3)               | 13 (6.7)         | 0.921   |
| History of atrial fibrillation, N (%) | 21 (3.5)    | 11 (1.6)               | 4 (2.1)          | 0.091   |
| Antihypertensive medication    |                  |                        |                  |         |
| RASB, N (%)                    | 441 (73.1)       | 538 (79.1)             | 156 (80.8)       | 0.015   |
| RASB duration, day             | 1707.7±1218.9    | 1873.5±1204.8          | 1889.5±1159.9    | 0.040   |
| BB, N (%)                      | 185 (30.7)       | 201 (29.6)             | 74 (38.3)        | 0.063   |
| BB duration, day               | 1073.3±1143.7    | 988.5±1078.0           | 1088.3±1089.8    | 0.525   |
| CCB, N (%)                     | 423 (70.1)       | 539 (79.3)             | 155 (80.3)       | <0.001  |
| CCB duration, day              | 1727.7±1286.6    | 1953.2±1246.5          | 2002.5±1271.4    | 0.004   |
| Diuretics, N (%)               | 158 (26.2)       | 232 (34.1)             | 60 (31.1)        | 0.009   |
| Diuretics duration, day        | 905.3±929.8      | 880.1±895.3            | 936.4±967.8      | 0.839   |
| Statin, N (%)                  | 424 (70.3)       | 452 (66.5)             | 123 (63.7)       | 0.154   |
| Statin duration, day           | 1627.7±1024.7    | 1467.5±994.0           | 1544.0±1045.8    | 0.043   |
| Aspirin, N (%)                 | 432 (71.6)       | 466 (68.5)             | 132 (68.4)       | 0.434   |
| Duration                        | BB  | BP  | CCB | DM  | RASB | SBP  | P-value |
|--------------------------------|-----|-----|-----|-----|------|------|---------|
| Aspirin duration, day          | 1305.9±970.3 | 1215.8±889.3 | 1176.1±859.0 | 0.160 |
| Follow-up duration, day        | 3160.1±554.4 | 3076.4±586.2 | 2991.6±716.4 | 0.001 |

Data are presented as mean ± SD or N (%).

BB, beta blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; DM, diabetes mellitus; RASB, renin angiotensin system blocker; SBP, systolic blood pressure.
Table S3. Propensity-adjusted Cox proportional hazard models for mortality according to observed mean SBP groups in study population without baseline atrial fibrillation (<120 [N=760], 120 to <130 [N=774], ≥120 mmHg [N=728]).

| Event Type                      | SBP Group               | No. of events (%) | HR (95% CI)          | P value  |
|---------------------------------|-------------------------|-------------------|----------------------|----------|
| **All-cause death**             | <130 mmHg               | 100 (13.16)       | 0.63 (0.47-0.86)     | 0.003    |
|                                 | 130 to <140 mmHg        | 108 (13.95)       | 0.59 (0.46-0.77)     | <0.001   |
|                                 | ≥140 mmHg               | 183 (25.14)       | reference            | reference|
| **Cardiovascular death**        | <130 mmHg               | 37 (4.87)         | 0.52 (0.32-0.85)     | 0.009    |
|                                 | 130 to <140 mmHg        | 30 (3.88)         | 0.37 (0.23-0.58)     | <0.001   |
|                                 | ≥140 mmHg               | 80 (10.99)        | reference            | reference|
| **Fatal MI**                    | <130 mmHg               | 4 (0.53)          | 0.54 (0.13-2.24)     | 0.398    |
|                                 | 130 to <140 mmHg        | 4 (0.52)          | 0.42 (0.12-1.46)     | 0.172    |
|                                 | ≥140 mmHg               | 11 (1.51)         | reference            | reference|
| **Fatal hemorrhagic stroke**    | <130 mmHg               | 3 (0.39)          | 0.47 (0.11-2.02)     | 0.310    |
|                                 | 130 to <140 mmHg        | 4 (0.52)          | 0.38 (0.12-1.26)     | 0.115    |
|                                 | ≥140 mmHg               | 14 (1.92)         | reference            | reference|
| **Fatal ischemic stroke**       | <130 mmHg               | 5 (0.66)          | 0.19 (0.06-0.62)     | 0.006    |
|                                 | 130 to <140 mmHg        | 5 (0.65)          | 0.20 (0.07-0.56)     | 0.002    |
|                                 | ≥140 mmHg               | 20 (2.75)         | reference            | reference|
| **Non-fatal MI**                | <130 mmHg               | 22 (2.89)         | 1.97 (0.86-4.50)     | 0.109    |
|                                 | 130 to <140 mmHg        | 15 (1.94)         | 1.11 (0.51-2.41)     | 0.796    |
|                                 | ≥140 mmHg               | 17 (2.34)         | reference            | reference|
| **Non-fatal hemorrhagic stroke**| <130 mmHg               | 35 (4.61)         | 0.57 (0.34-0.97)     | 0.040    |
|                                 | 130 to <140 mmHg        | 44 (5.68)         | 0.74 (0.47-1.16)     | 0.188    |
|                                 | ≥140 mmHg               | 54 (7.42)         | reference            | reference|
| **Non-fatal ischemic stroke**   | <130 mmHg               | 163 (21.45)       | 0.93 (0.71-1.22)     | 0.601    |
|                                 | 130 to <140 mmHg        | 168 (21.71)       | 0.93 (0.74-1.18)     | 0.558    |
|                                 | ≥140 mmHg               | 174 (23.90)       | reference            | reference|

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

SBP, systolic blood pressure; MI, myocardial infarction.
Table S4. Propensity-adjusted Cox proportional hazard models for mortality according to observed mean DBP groups in study population without baseline atrial fibrillation (<80 [N=848], 80 to <90 [N=1080], ≥90 mmHg [N=334]).

|                          | No. of events (%) | HR (95% CI)         | P value |
|--------------------------|-------------------|---------------------|---------|
| All-cause death          |                   |                     |         |
| <80 mmHg                 | 122 (14.39)       | 0.43 (0.31-0.61)    | <0.001  |
| 80 to <90 mmHg           | 186 (17.22)       | 0.59 (0.44-0.78)    | <0.001  |
| ≥90 mmHg                 | 83 (24.85)        | reference           |         |
| Cardiovascular death     |                   |                     |         |
| <80 mmHg                 | 39 (4.60)         | 0.26 (0.15-0.45)    | <0.001  |
| 80 to <90 mmHg           | 68 (6.30)         | 0.44 (0.28-0.68)    | <0.001  |
| ≥90 mmHg                 | 40 (11.98)        | reference           |         |
| Fatal MI                 |                   |                     |         |
| <80 mmHg                 | 2 (0.24)          | 0.04 (0.01-0.28)    | 0.001   |
| 80 to <90 mmHg           | 10 (0.93)         | 0.31 (0.10-0.95)    | 0.041   |
| ≥90 mmHg                 | 7 (2.10)          | reference           |         |
| Fatal hemorrhagic stroke |                   |                     |         |
| <80 mmHg                 | 4 (0.47)          | 0.20 (0.04-0.92)    | 0.039   |
| 80 to <90 mmHg           | 9 (0.83)          | 0.37 (0.13-1.09)    | 0.072   |
| ≥90 mmHg                 | 8 (2.40)          | reference           |         |
| Fatal ischemic stroke    |                   |                     |         |
| <80 mmHg                 | 8 (0.94)          | 0.20 (0.06-0.66)    | 0.008   |
| 80 to <90 mmHg           | 14 (1.30)         | 0.36 (0.14-0.94)    | 0.036   |
| ≥90 mmHg                 | 8 (2.40)          | reference           |         |
| Nonfatal MI              |                   |                     |         |
| <80 mmHg                 | 26 (3.07)         | 1.33 (0.54-3.30)    | 0.532   |
| 80 to <90 mmHg           | 18 (1.67)         | 0.58 (0.25-1.36)    | 0.211   |
| ≥90 mmHg                 | 10 (2.99)         | reference           |         |
| Non-fatal hemorrhagic stroke |              |                     |         |
| <80 mmHg                 | 40 (4.72)         | 0.48 (0.26-0.87)    | 0.016   |
| 80 to <90 mmHg           | 63 (5.83)         | 0.65 (0.40-1.06)    | 0.085   |
| ≥90 mmHg                 | 30 (8.98)         | reference           |         |
| Non-fatal ischemic stroke|                   |                     |         |
| <80 mmHg                 | 186 (21.93)       | 0.78 (0.57-1.06)    | 0.116   |
| 80 to <90 mmHg           | 237 (21.94)       | 0.80 (0.61-1.05)    | 0.106   |
| ≥90 mmHg                 | 82 (24.55)        | reference           |         |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

DBP, diastolic blood pressure; MI, myocardial infarction.
Table S5. Propensity-adjusted Cox proportional hazard models for clinical events according to observed mean SBP groups in study population including subjects with antihypertensive medication duration <1 year (<120 [N=927], 120 to <130 [N=880], ≥120 mmHg [N=835]).

| Event Type                  | SBP Group       | No. of events (%) | Adjusted HR (95% CI) | P value |
|-----------------------------|-----------------|-------------------|----------------------|---------|
| **All-cause death**         | <130 mmHg       | 150 (16.18)       | 0.58 (0.45-0.75)     | <0.001  |
|                             | 130 to <140 mmHg | 150 (17.05)       | 0.57 (0.45-0.71)     | <0.001  |
|                             | ≥140 mmHg       | 248 (29.70)       | reference            | reference|
| **Cardiovascular death**    | <130 mmHg       | 60 (6.47)         | 0.52 (0.34-0.78)     | 0.002   |
|                             | 130 to <140 mmHg| 50 (5.68)         | 0.43 (0.30-0.63)     | 0.000   |
|                             | ≥140 mmHg       | 110 (13.17)       | reference            | reference|
| **Fatal MI**                | <130 mmHg       | 6 (0.65)          | 0.29 (0.09-1.00)     | 0.050   |
|                             | 130 to <140 mmHg| 5 (0.57)          | 0.29 (0.10-0.87)     | 0.027   |
|                             | ≥140 mmHg       | 16 (1.92)         | reference            | reference|
| **Fatal hemorrhagic stroke**| <130 mmHg       | 9 (0.97)          | 0.89 (0.32-2.50)     | 0.823   |
|                             | 130 to <140 mmHg| 5 (0.57)          | 0.36 (0.13-1.04)     | 0.059   |
|                             | ≥140 mmHg       | 20 (2.40)         | reference            | reference|
| **Fatal ischemic stroke**   | <130 mmHg       | 9 (0.97)          | 0.20 (0.08-0.49)     | <0.001  |
|                             | 130 to <140 mmHg| 12 (1.36)         | 0.31 (0.15-0.65)     | 0.002   |
|                             | ≥140 mmHg       | 29 (3.47)         | reference            | reference|
| **Non-fatal MI**            | <130 mmHg       | 25 (2.70)         | 2.01 (0.90-4.50)     | 0.090   |
|                             | 130 to <140 mmHg| 17 (1.93)         | 1.23 (0.58-2.60)     | 0.587   |
|                             | ≥140 mmHg       | 18 (2.16)         | reference            | reference|
| **Non-fatal hemorrhagic stroke** | <130 mmHg     | 43 (4.64)         | 0.63 (0.39-1.03)     | 0.066   |
|                             | 130 to <140 mmHg| 48 (5.45)         | 0.72 (0.48-1.09)     | 0.124   |
|                             | ≥140 mmHg       | 66 (7.90)         | reference            | reference|
| **Non-fatal ischemic stroke**| <130 mmHg       | 198 (21.36)       | 0.95 (0.74-1.22)     | 0.695   |
|                             | 130 to <140 mmHg| 189 (21.48)       | 0.94 (0.75-1.18)     | 0.604   |
|                             | ≥140 mmHg       | 196 (23.47)       | reference            | reference|

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

SBP, systolic blood pressure; MI, myocardial infarction.
Table S6. Propensity-adjusted Cox proportional hazard models for clinical events according to observed mean DBP groups in study population including subjects with antihypertensive medication duration <1 year (<80 [N=1020], 80 to <90 [N=1230], ≥90 mmHg [N=392]).

| Event Type                          | DBP Group | No. of Events (%) | Adjusted HR (95% CI)        | P value |
|-------------------------------------|-----------|-------------------|----------------------------|---------|
| **All-cause death**                 |           |                   |                            |         |
| <80 mmHg                            | 184 (18.04) | 0.42 (0.31-0.56)  | <0.001                     |         |
| 80 to <90 mmHg                      | 245 (19.92) | 0.53 (0.42-0.68)  | <0.001                     |         |
| ≥90 mmHg                            | 119 (30.36) | reference         | reference                  |         |
| **Cardiovascular death**            |           |                   |                            |         |
| <80 mmHg                            | 67 (6.57)  | 0.32 (0.20-0.50)  | <0.001                     |         |
| 80 to <90 mmHg                      | 96 (7.80)  | 0.45 (0.31-0.65)  | <0.001                     |         |
| ≥90 mmHg                            | 57 (14.54) | reference         | reference                  |         |
| **Fatal MI**                        |           |                   |                            |         |
| <80 mmHg                            | 4 (0.39)   | 0.08 (0.02-0.35)  | 0.001                      |         |
| 80 to <90 mmHg                      | 14 (1.14)  | 0.38 (0.15-1.00)  | 0.050                      |         |
| ≥90 mmHg                            | 9 (2.30)   | reference         | reference                  |         |
| **Fatal hemorrhagic stroke**        |           |                   |                            |         |
| <80 mmHg                            | 7 (0.69)   | 0.25 (0.07-0.81)  | 0.021                      |         |
| 80 to <90 mmHg                      | 15 (1.22)  | 0.44 (0.19-1.04)  | 0.062                      |         |
| ≥90 mmHg                            | 12 (3.06)  | reference         | reference                  |         |
| **Fatal ischemic stroke**           |           |                   |                            |         |
| <80 mmHg                            | 13 (1.27)  | 0.22 (0.09-0.57)  | 0.002                      |         |
| 80 to <90 mmHg                      | 23 (1.87)  | 0.40 (0.19-0.84)  | 0.015                      |         |
| ≥90 mmHg                            | 14 (3.57)  | reference         | reference                  |         |
| **Non-fatal MI**                    |           |                   |                            |         |
| <80 mmHg                            | 30 (2.94)  | 1.41 (0.59-3.38)  | 0.439                      |         |
| 80 to <90 mmHg                      | 19 (1.54)  | 0.59 (0.26-1.34)  | 0.211                      |         |
| ≥90 mmHg                            | 11 (2.81)  | reference         | reference                  |         |
| **Non-fatal hemorrhagic stroke**    |           |                   |                            |         |
| <80 mmHg                            | 47 (4.61)  | 0.48 (0.28-0.83)  | 0.009                      |         |
| 80 to <90 mmHg                      | 72 (5.85)  | 0.64 (0.41-1.00)  | 0.050                      |         |
| ≥90 mmHg                            | 38 (9.69)  | reference         | reference                  |         |
| **Non-fatal ischemic stroke**       |           |                   |                            |         |
| <80 mmHg                            | 223 (21.86)| 0.80 (0.60-1.07)  | 0.135                      |         |
| 80 to <90 mmHg                      | 264 (21.46)| 0.80 (0.62-1.03)  | 0.083                      |         |
| ≥90 mmHg                            | 96 (24.49) | reference         | reference                  |         |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

DBP, diastolic blood pressure; MI, myocardial infarction.
| Event Type                  | SBP Group           | No. of Events (%) | Adjusted HR (95% CI) | P value  |
|-----------------------------|---------------------|-------------------|----------------------|----------|
| **All-cause death**         | <130 mmHg           | 98 (12.52)        | 0.71 (0.52-0.97)     | 0.032    |
|                             | 130 to <140 mmHg    | 108 (13.71)       | 0.68 (0.52-0.89)     | 0.005    |
|                             | ≥140 mmHg           | 160 (22.54)       | reference            | reference|
| **Cardiovascular death**    | <130 mmHg           | 37 (4.73)         | 0.65 (0.39-1.08)     | 0.093    |
|                             | 130 to <140 mmHg    | 31 (3.93)         | 0.47 (0.29-0.75)     | 0.001    |
|                             | ≥140 mmHg           | 63 (8.87)         | reference            | reference|
| **Fatal MI**                | <130 mmHg           | 4 (0.51)          | 0.67 (0.15-3.05)     | 0.606    |
|                             | 130 to <140 mmHg    | 3 (0.38)          | 0.41 (0.10-1.69)     | 0.216    |
|                             | ≥140 mmHg           | 8 (1.13)          | reference            | reference|
| **Fatal hemorrhagic stroke**| <130 mmHg           | 3 (0.38)          | 0.66 (0.14-3.13)     | 0.598    |
|                             | 130 to <140 mmHg    | 4 (0.51)          | 0.57 (0.16-2.03)     | 0.383    |
|                             | ≥140 mmHg           | 9 (1.27)          | reference            | reference|
| **Fatal ischemic stroke**   | <130 mmHg           | 3 (0.38)          | 0.16 (0.04-0.67)     | 0.012    |
|                             | 130 to <140 mmHg    | 6 (0.76)          | 0.31 (0.11-0.85)     | 0.023    |
|                             | ≥140 mmHg           | 14 (1.97)         | reference            | reference|
| **Non-fatal MI**            | <130 mmHg           | 22 (2.8)          | 1.95 (0.86-4.45)     | 0.111    |
|                             | 130 to <140 mmHg    | 16 (2.0)          | 1.16 (0.54-2.50)     | 0.699    |
|                             | ≥140 mmHg           | 17 (2.4)          | reference            | reference|
| **Non-fatal hemorrhagic stroke** | <130 mmHg           | 35 (4.5)         | 0.57 (0.37-0.87)     | 0.010    |
|                             | 130 to <140 mmHg    | 45 (5.7)          | 0.74 (0.50-1.11)     | 0.150    |
|                             | ≥140 mmHg           | 52 (7.3)          | reference            | reference|
| **Non-fatal ischemic stroke** | <130 mmHg           | 170 (21.7)       | 0.91 (0.70-1.19)     | 0.508    |
|                             | 130 to <140 mmHg    | 173 (22.0)        | 0.91 (0.72-1.15)     | 0.437    |
|                             | ≥140 mmHg           | 175 (24.7)        | reference            | reference|

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

SBP, systolic blood pressure; MI, myocardial infarction.
Table S8. Propensity-adjusted Cox proportional hazard models for mortality according to observed mean DBP groups in survivors after 1 year from the index stroke event (<80 [N=870], 80 to <90 [N=1086], ≥90 mmHg [N=325]).

|                  | No. of events (%) | Adjusted HR (95% CI) | P value |
|------------------|-------------------|----------------------|---------|
| **All-cause death** |                   |                      |         |
| <80 mmHg         | 120 (13.79)       | 0.53 (0.37-0.77)     | <0.001  |
| 80 to <90 mmHg   | 177 (16.30)       | 0.69 (0.51-0.94)     | 0.020   |
| ≥90 mmHg         | 69 (21.23)        | reference            |         |
| **Cardiovascular death** |       |                      |         |
| <80 mmHg         | 39 (4.48)         | 0.35 (0.19-0.62)     | <0.001  |
| 80 to <90 mmHg   | 61 (5.62)         | 0.50 (0.31-0.81)     | 0.005   |
| ≥90 mmHg         | 31 (9.54)         | reference            |         |
| **Fatal MI**     |                   |                      |         |
| <80 mmHg         | 2 (0.23)          | 0.05 (0.01-0.36)     | 0.003   |
| 80 to <90 mmHg   | 8 (0.74)          | 0.31 (0.09-1.18)     | 0.073   |
| ≥90 mmHg         | 5 (1.54)          | reference            |         |
| **Fatal hemorrhagic stroke** |     |                      |         |
| <80 mmHg         | 3 (0.34)          | 0.16 (0.03-0.90)     | 0.038   |
| 80 to <90 mmHg   | 7 (0.64)          | 0.33 (0.10-1.10)     | 0.071   |
| ≥90 mmHg         | 6 (1.85)          | reference            |         |
| **Fatal ischemic stroke** |     |                      |         |
| <80 mmHg         | 7 (0.80)          | 0.44 (0.10-1.99)     | 0.289   |
| 80 to <90 mmHg   | 13 (1.20)         | 0.73 (0.20-2.70)     | 0.641   |
| ≥90 mmHg         | 3 (0.92)          | reference            |         |
| **Non-fatal MI** |                   |                      |         |
| <80 mmHg         | 27 (3.1)          | 1.33 (0.54-3.29)     | 0.533   |
| 80 to <90 mmHg   | 18 (1.7)          | 0.57 (0.24-1.32)     | 0.187   |
| ≥90 mmHg         | 10 (3.1)          | reference            |         |
| **Non-fatal hemorrhagic stroke** |     |                      |         |
| <80 mmHg         | 40 (4.6)          | 0.50 (0.31-0.80)     | 0.004   |
| 80 to <90 mmHg   | 63 (5.8)          | 0.64 (0.41-1.00)     | 0.050   |
| ≥90 mmHg         | 29 (8.9)          | reference            |         |
| **Non-fatal ischemic stroke** |     |                      |         |
| <80 mmHg         | 193 (22.2)        | 0.76 (0.56-1.04)     | 0.088   |
| 80 to <90 mmHg   | 242 (22.3)        | 0.79 (0.60-1.04)     | 0.089   |
| ≥90 mmHg         | 83 (25.5)         | reference            |         |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

DBP, diastolic blood pressure; MI, myocardial infarction.
Table S9. Propensity-adjusted Cox proportional hazard models for clinical events in 4 groups by mean SBP (<120 [N=199], 120 to <130 [N=592], 130 to <140 [N=793], ≥140 mmHg [N=736]).

| Event Type                      | Group            | No. of events (%) | Adjusted HR (95% CI) | P value  | Adjusted HR (95% CI) | P value  |
|---------------------------------|------------------|-------------------|----------------------|----------|----------------------|----------|
|                                 | <120 mmHg        | 29 (14.57)        | 0.76 (0.46-1.23)     | 0.260    | 1.23 (0.77-1.98)     | 0.381    |
| All-cause death                 | 120 to <130 mmHg | 77 (13.01)        | 0.63 (0.46-0.86)     | 0.004    | 1.03 (0.76-1.39)     | 0.845    |
|                                 | 130 to <140 mmHg | 113 (14.25)       | 0.61 (0.47-0.79)     | <0.001   | reference            | reference|
|                                 | ≥140 mmHg        | 186 (25.27)       | reference            | reference| 1.63 (1.26-2.11)     | <0.001   |
|                                 |                  |                   |                      |          |                      |          |
| Cardiovascular death            | <120 mmHg        | 8 (4.02)          | 0.46 (0.20-1.09)     | 0.077    | 1.18 (0.50-2.76)     | 0.709    |
|                                 | 120 to <130 mmHg | 34 (5.74)         | 0.59 (0.36-0.95)     | 0.031    | 1.50 (0.91-2.45)     | 0.109    |
|                                 | 130 to <140 mmHg | 33 (4.16)         | 0.39 (0.25-0.61)     | <0.001   | reference            | reference|
|                                 | ≥140 mmHg        | 81 (11.01)        | reference            | reference| 2.54 (1.64-3.95)     | <0.001   |
| Fatal MI                        | <120 mmHg        | 0 (0.00)          | x                    | x        | x                    | x        |
|                                 | 120 to <130 mmHg | 4 (0.68)          | x                    | x        | x                    | x        |
|                                 | 130 to <140 mmHg | 4 (0.50)          | x                    | x        | reference            | reference|
|                                 | ≥140 mmHg        | 11 (1.49)         | reference            | reference| x                    | x        |
| Fatal hemorrhagic stroke        | <120 mmHg        | 1 (0.50)          | 0.96 (0.07-12.49)    | 0.978    | 2.46 (0.18-33.10)    | 0.496    |
|                                 | 120 to <130 mmHg | 2 (0.34)          | 0.41 (0.08-2.07)     | 0.279    | 1.04 (0.18-5.89)     | 0.963    |
|                                 | 130 to <140 mmHg | 4 (0.50)          | 0.39 (0.12-1.27)     | 0.118    | reference            | reference|
|                                 | ≥140 mmHg        | 14 (1.90)         | reference            | reference| 2.56 (0.79-8.28)     | 0.118    |
| Fatal ischemic stroke           | <120 mmHg        | 1 (0.50)          | 0.14 (0.02-1.31)     | 0.085    | 0.59 (0.06-5.36)     | 0.637    |
|                                 | 120 to <130 mmHg | 6 (1.01)          | 0.26 (0.09-0.75)     | 0.012    | 1.06 (0.35-3.23)     | 0.921    |
|                                 | 130 to <140 mmHg | 7 (0.88)          | 0.25 (0.10-0.62)     | 0.003    | reference            | reference|
|                                 | ≥140 mmHg        | 21 (2.85)         | reference            | reference| 4.07 (1.62-10.23)    | 0.003    |
| Non-fatal MI                    | <120 mmHg        | 5 (2.51)          | 2.03 (0.59-7.01)     | 0.262    | 1.72 (0.55-5.37)     | 0.352    |
| SBP, mmHg | Reference Group | Hazard Ratio (95% CI) | p-value | Hazard Ratio (95% CI) | p-value |
|-----------|-----------------|----------------------|---------|----------------------|---------|
| 120 to <130 mmHg | 17 (2.87) | 1.98 (0.86-4.57) | 0.108 | 1.68 (0.83-3.41) | 0.153 |
| 130 to <140 mmHg | 16 (2.02) | 1.18 (0.55-2.53) | 0.668 | reference | reference |
| ≥140 mmHg | 17 (2.31) | reference | reference | 0.85 (0.39-1.82) | 0.668 |
| Non-fatal hemorrhagic stroke | | | | | |
| <120 mmHg | 9 (4.52) | 0.56 (0.24-1.31) | 0.185 | 0.74 (0.34-1.65) | 0.468 |
| 120 to <130 mmHg | 26 (4.39) | 0.57 (0.33-0.99) | 0.046 | 0.75 (0.46-1.24) | 0.259 |
| 130 to <140 mmHg | 45 (5.67) | 0.76 (0.49-1.18) | 0.222 | reference | reference |
| ≥140 mmHg | 54 (7.34) | reference | reference | 1.32 (0.85-2.05) | 0.222 |
| Non-fatal ischemic stroke | | | | | |
| <120 mmHg | 5 (2.51) | 1.10 (0.74-1.64) | 0.626 | 1.20 (0.83-1.72) | 0.336 |
| 120 to <130 mmHg | 17 (2.87) | 0.88 (0.67-1.16) | 0.360 | 0.95 (0.75-1.21) | 0.697 |
| 130 to <140 mmHg | 16 (2.02) | 0.92 (0.73-1.16) | 0.497 | reference | reference |
| ≥140 mmHg | 17 (2.31) | reference | reference | 1.08 (0.86-1.37) | 0.497 |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

SBP, systolic blood pressure; MI, myocardial infarction.
Table S10. Propensity-adjusted Cox proportional hazard models for clinical events in 4 groups by mean DBP (<70 [N=92], 70 to <80 [N=786], 80 to <90 [N=1100], ≥90 mmHg [N=342]).

| Event Type                  | Group          | No. of events (%) | Adjusted HR (95% CI) | P value | Adjusted HR (95% CI) | P value |
|-----------------------------|----------------|-------------------|----------------------|---------|----------------------|---------|
|                             |                |                   |                      |         |                      |         |
| All-cause death             | <70 mmHg       | 14 (15.22)        | 0.76 (0.41-1.41)     | 0.383   | 0.98 (0.54-1.75)     | 0.934   |
|                             | 70 to <80 mmHg | 114 (14.50)       | 0.70 (0.51-0.94)     | 0.020   | 0.89 (0.70-1.13)     | 0.356   |
|                             | 80 to <90 mmHg | 191 (17.36)       | 0.78 (0.60-1.02)     | 0.065   | reference            | reference |
|                             | ≥90 mmHg       | 86 (25.15)        | reference            | reference | 1.28 (0.98-1.68) | 0.065   |
| Cardiovascular death        | <70 mmHg       | 3 (3.26)          | 0.34 (0.10-1.16)     | 0.086   | 0.59 (0.18-1.96)     | 0.389   |
|                             | 70 to <80 mmHg | 40 (5.09)         | 0.48 (0.30-0.78)     | 0.003   | 0.84 (0.56-1.25)     | 0.392   |
|                             | 80 to <90 mmHg | 71 (6.45)         | 0.57 (0.38-0.86)     | 0.007   | reference            | reference |
|                             | ≥90 mmHg       | 42 (12.28)        | reference            | reference | 1.74 (1.17-2.60) | 0.007   |
| Fatal MI                    | <70 mmHg       | 0 (0.00)          | x                    | x       | x                    | x       |
|                             | 70 to <80 mmHg | 2 (0.25)          | x                    | x       | X                    | x       |
|                             | 80 to <90 mmHg | 10 (0.91)         | x                    | x       | reference            | reference |
|                             | ≥90 mmHg       | 7 (2.05)          | reference            | reference | x                    | x       |
| Fatal hemorrhagic stroke    | <70 mmHg       | 0 (0.00)          | x                    | x       | \x                   | x       |
|                             | 70 to <80 mmHg | 4 (0.51)          | x                    | x       | x                    | x       |
|                             | 80 to <90 mmHg | 9 (0.82)          | x                    | x       | reference            | reference |
|                             | ≥90 mmHg       | 8 (2.34)          | reference            | reference | x                    | x       |
| Fatal ischemic stroke       | <70 mmHg       | 1 (1.09)          | 0.48 (0.05-4.22)     | 0.507   | 0.97 (0.12-7.87)     | 0.976   |
|                             | 70 to <80 mmHg | 8 (1.02)          | 0.36 (0.13-1.00)     | 0.051   | 0.73 (0.31-1.75)     | 0.484   |
|                             | 80 to <90 mmHg | 16 (1.45)         | 0.49 (0.22-1.14)     | 0.098   | reference            | reference |
|                             | ≥90 mmHg       | 10 (2.92)         | reference            | reference | 2.02 (0.88-4.65) | 0.098   |
| Non-fatal MI                | <70 mmHg       | 2 (2.17)          | 1.09 (0.21-5.56)     | 0.922   | 1.67 (0.36-7.75)     | 0.513   |
| SBP Range         | Cases  | Hazard Ratio (95%CI) | P-value | Reference Hazard Ratio (95%CI) |
|-------------------|--------|----------------------|---------|-------------------------------|
| 70 to <80 mmHg    | 25 (3.18) | 1.40 (0.62-3.16) | 0.414   | 2.16 (1.16-4.02) | 0.016 |
| 80 to <90 mmHg    | 18 (1.64) | 0.65 (0.29-1.45) | 0.294   | reference                     | reference |
| ≥90 mmHg          | 10 (2.92) | reference            | reference | 1.54 (0.69-3.44) | 0.294 |

**Non-fatal hemorrhagic stroke**

| SBP Range         | Cases  | Hazard Ratio (95%CI) | P-value | Reference Hazard Ratio (95%CI) |
|-------------------|--------|----------------------|---------|-------------------------------|
| <70 mmHg          | 4 (4.35) | 0.48 (0.16-1.48) | 0.202   | 0.72 (0.25-2.10) | 0.551 |
| 70 to <80 mmHg    | 36 (4.58) | 0.52 (0.30-0.88) | 0.015   | 0.77 (0.51-1.18) | 0.233 |
| 80 to <90 mmHg    | 64 (5.82) | 0.67 (0.42-1.05) | 0.081   | reference                     | reference |
| ≥90 mmHg          | 30 (8.77) | reference            | reference | 1.50 (0.95-2.37) | 0.081 |

**Non-fatal ischemic stroke**

| SBP Range         | Cases  | Hazard Ratio (95%CI) | P-value | Reference Hazard Ratio (95%CI) |
|-------------------|--------|----------------------|---------|-------------------------------|
| <70 mmHg          | 17 (18.48) | 0.75 (0.43-1.30) | 0.301   | 0.86 (0.51-1.43) | 0.555 |
| 70 to <80 mmHg    | 176 (22.39) | 0.89 (0.67-1.18) | 0.412   | 1.02 (0.84-1.25) | 0.840 |
| 80 to <90 mmHg    | 243 (22.09) | 0.87 (0.67-1.13) | 0.291   | reference                     | reference |
| ≥90 mmHg          | 87 (25.44) | reference            | reference | 1.15 (0.89-1.48) | 0.291 |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

SBP, systolic blood pressure; MI, myocardial infarction.
Table S11. Propensity-adjusted Cox proportional hazard models for mortality according to SBP groups using last BP (<120 [N=718], 120 to <130 [N=633], ≥120 mmHg [N=969]).

| Category                  | SBP Groups          | No. of events (%) | HR (95% CI)      | P value |
|---------------------------|---------------------|-------------------|------------------|---------|
| All-cause death           | <130 mmHg           | 143 (14.8)        | 0.80 (0.64-1.01) | 0.066   |
|                           | 130 to <140 mmHg    | 101 (16.0)        | 0.76 (0.59-0.98) | 0.033   |
|                           | ≥140 mmHg           | 161 (22.4)        | reference        | reference |
| Cardiovascular death      | <130 mmHg           | 52 (5.4)          | 0.69 (0.48-1.00) | 0.052   |
|                           | 130 to <140 mmHg    | 35 (5.5)          | 0.64 (0.42-0.96) | 0.030   |
|                           | ≥140 mmHg           | 69 (9.6)          | reference        | reference |
| Fatal MI                  | <130 mmHg           | 6 (0.6)           | 0.58 (0.21-1.65) | 0.309   |
|                           | 130 to <140 mmHg    | 3 (0.5)           | 0.38 (0.10-1.39) | 0.145   |
|                           | ≥140 mmHg           | 10 (1.4)          | reference        | reference |
| Fatal hemorrhagic stroke  | <130 mmHg           | 3 (0.3)           | 0.27 (0.07-1.00) | 0.050   |
|                           | 130 to <140 mmHg    | 7 (1.1)           | 0.82 (0.31-2.13) | 0.681   |
|                           | ≥140 mmHg           | 11 (1.5)          | reference        | reference |
| Fatal ischemic stroke     | <130 mmHg           | 6 (0.6)           | 0.23 (0.09-0.58) | 0.002   |
|                           | 130 to <140 mmHg    | 7 (1.1)           | 0.42 (0.18-0.98) | 0.046   |
|                           | ≥140 mmHg           | 22 (3.1)          | reference        | reference |
| Non-fatal MI              | <130 mmHg           | 30 (3.1)          | 1.37 (0.75-2.50) | 0.304   |
|                           | 130 to <140 mmHg    | 7 (1.1)           | 0.44 (0.18-1.05) | 0.065   |
|                           | ≥140 mmHg           | 18 (2.5)          | reference        | reference |
| Non-fatal hemorrhagic stroke | <130 mmHg       | 51 (5.3)          | 0.87 (0.58-1.32) | 0.526   |
|                           | 130 to <140 mmHg    | 40 (6.3)          | 1.04 (0.67-1.60) | 0.865   |
|                           | ≥140 mmHg           | 43 (6.0)          | reference        | reference |
| Non-fatal ischemic stroke | <130 mmHg           | 218 (22.5)        | 1.12 (0.91-1.38) | 0.285   |
|                           | 130 to <140 mmHg    | 147 (23.2)        | 1.10 (0.88-1.38) | 0.419   |
|                           | ≥140 mmHg           | 158 (22.0)        | reference        | reference |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.
SBP, systolic blood pressure; MI, myocardial infarction.
Table S12. Propensity-adjusted Cox proportional hazard models for mortality according to DBP groups using last BP (<80 [N=978], 80 to <90 [N=871], ≥90 mmHg [N=471]).

| Event Type                        | DBP Group       | No. of events (%) | HR (95% CI)       | P value |
|-----------------------------------|-----------------|-------------------|-------------------|---------|
| All-cause death                   | <80 mmHg        | 158 (18.1)        | 0.79 (0.61-1.03)  | 0.080   |
|                                   | 80 to <90 mmHg  | 98 (20.8)         | 0.94 (0.73-1.22)  | 0.657   |
|                                   | ≥90 mmHg        | 49 (5.01)         | reference         | reference |
| Cardiovascular death              | <80 mmHg        | 61 (7.0)          | 0.59 (0.39-0.89)  | 0.011   |
|                                   | 80 to <90 mmHg  | 46 (9.8)          | 0.82 (0.55-1.20)  | 0.301   |
|                                   | ≥90 mmHg        | 1 (0.1)           | reference         | reference |
| Fatal MI                          | <80 mmHg        | 10 (1.2)          | 0.06 (0.01-0.50)  | 0.009   |
|                                   | 80 to <90 mmHg  | 8 (1.7)           | 0.76 (0.29-1.94)  | 0.560   |
|                                   | ≥90 mmHg        | 4 (0.4)           | reference         | reference |
| Fatal hemorrhagic stroke          | <80 mmHg        | 10 (1.2)          | 0.36 (0.10-1.26)  | 0.111   |
|                                   | 80 to <90 mmHg  | 7 (1.5)           | 0.92 (0.35-2.44)  | 0.866   |
|                                   | ≥90 mmHg        | 12 (1.2)          | reference         | reference |
| Fatal ischemic stroke             | <80 mmHg        | 10 (1.6)          | 0.46 (0.21-1.03)  | 0.060   |
|                                   | 80 to <90 mmHg  | 13 (2.8)          | 0.47 (0.20-1.07)  | 0.073   |
|                                   | ≥90 mmHg        | 26 (2.7)          | reference         | reference |
| Non-fatal MI                      | <80 mmHg        | 16 (1.8)          | 1.31 (0.72-2.37)  | 0.380   |
|                                   | 80 to <90 mmHg  | 13 (2.8)          | 0.44 (0.18-1.06)  | 0.067   |
|                                   | ≥90 mmHg        | 40 (4.1)          | reference         | reference |
| Non-fatal hemorrhagic stroke      | <80 mmHg        | 64 (7.3)          | 0.91 (0.60-1.37)  | 0.643   |
|                                   | 80 to <90 mmHg  | 30 (6.4)          | 1.05 (0.68-1.62)  | 0.823   |
|                                   | ≥90 mmHg        | 221 (22.6)        | reference         | reference |
| Non-fatal ischemic stroke         | <80 mmHg        | 190 (21.8)        | 1.08 (0.88-1.33)  | 0.442   |
|                                   | 80 to <90 mmHg  | 112 (23.8)        | 1.08 (0.86-1.35)  | 0.500   |
|                                   | ≥90 mmHg        | 158 (18.1)        | reference         | reference |

All models were adjusted by propensity scores based on age, sex, residential area, household income, smoking status, alcohol frequency, body mass index, total cholesterol, fasting glucose, baseline systolic blood pressure, baseline diastolic blood pressure, history of diabetes mellitus, and history atrial fibrillation.

DBP, diastolic blood pressure; MI, myocardial infarction.
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