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ORIGINAL RESEARCH

One-Year Blood Pressure Trajectory After Acute Ischemic Stroke

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BACKGROUND: Although the effect of blood pressure on poststroke outcome is well recognized, the long-term trajectory of blood pressure after acute ischemic stroke and its influence on outcomes have not been studied well.

METHODS AND RESULTS: We analyzed systolic blood pressure (SBP) measurements in 5514 patients with acute ischemic stroke at ≥2 of 7 prespecified time points during the first year after stroke among those enrolled in a multicenter prospective registry. Longitudinal SBPs were categorized using a group-based trajectory model. The primary outcome was a composite of stroke recurrence, myocardial infarction, and all-cause mortality up to 1 year after stroke. The study subjects were categorized into 4 SBP trajectory groups: *low* (27.0%), *moderate* (59.5%), *persistently high* (1.2%), and *slowly dropping* (12.4%). In the first 3 groups, SBP decreased during the first 3 to 7 days and remained steady thereafter. In the *slowly dropping SBP group*, SBPs decreased from 182 to 135 mm Hg during the first 30 days, then paralleled the trajectory of the *moderate SBP group*. Compared with the reference, the *moderate SBP group*, the *slowly dropping SBP group* was at higher risk for the primary outcome (adjusted hazard ratio [HR], 1.32; 95% CI, 1.05–1.65) and mortality (adjusted HR, 1.35; 95% CI, 1.03–1.78). Primary outcome rates were similarly high in the *persistently high SBP group*.

CONCLUSIONS: Four 1-year longitudinal SBP trajectories were identified in patients with acute ischemic stroke. Patients in the *slowly dropping SBP* and *persistently high SBP* trajectory groups were prone to adverse cardiovascular outcomes after stroke.

Key Words: acute ischemic stroke ■ blood pressure ■ cohort study ■ group-based trajectory model ■ prognosis

Clinicians are accustomed to managing blood pressure (BP) at one time point but may not consider longitudinal changes or BP trajectories over time.[1] The latter type of BP metrics are primarily based on community-indwelling cohorts and longitudinal BP changes over a lifetime. These studies have shown that individuals with sustained, poorly controlled high BP are at higher risk of cardiovascular events or mortality.[1–6]

Although elevation of BP after acute stroke is well known,[7] recent studies on BP trajectories after stroke show that BP changes during the acute period of

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CLINICAL PERSPECTIVE

What Is New?

- In a multicenter prospective registry of patients with acute ischemic stroke, a group-based trajectory model categorized participants into 4 systolic blood pressure (SBP) trajectory groups up to 1 year after stroke onset: *low SBP*, *moderate SBP*, *persistently high SBP*, and *slowly dropping SBP*.
- Patients in the *slowly dropping SBP* and *persistently high SBP* trajectory groups experienced more adverse cardiovascular events up to 1 year after stroke.
- More than half of the *slowly dropping SBP* and *persistently high SBP* trajectory groups received no antihypertensive medication or only one drug at 30 days after stroke onset.

What Are the Clinical Implications?

- SBP trajectory, especially in the early stage of ischemic stroke, might be a potential target for blood pressure–lowering interventions.
- Blood pressure lowering, particularly during the first 30 days after stroke onset, may improve outcomes in those in the *slowly dropping SBP* and *persistently high SBP* trajectory groups.

Nonstandard Abbreviation and Acronym

SBP	systolic blood pressure

stroke may have distinct patterns that are associated with prognosis.[8–10] Specifically, individuals with the distinctly high BP trajectory, whose BP does not drop or remains elevated during the first few hours after stroke onset, are more likely to have a poorer prognosis.[8] However, continuous observation about BP metrics and outcomes beyond the acute period of stroke is limited. Such knowledge is important as it may lead to more tailored BP management after stroke.

In this study, we aimed to describe the patterns of BP changes up to 1 year after ischemic stroke using group-based trajectory models and explore the associations between BP trajectory groups and poststroke cardiovascular outcomes.

METHODS

The anonymized data from this study may be shared after approval from the local institutional review board with qualified researchers performing legitimate research by contacting the lead investigator (H.-J.B. at braindoc@snu.ac.kr).

Study Subjects

Patients with acute ischemic stroke, who were admitted to the 10 participating centers of the CRCS-K (Clinical Research Collaboration for Stroke in Korea) registry[11,12] between January 2010 and December 2011 and who met the following eligibility criteria were considered for inclusion in the study: (1) hospitalization within 7 days of symptom onset (n=6547) and (2) documentation of ischemic lesions relevant to stroke symptoms on diffusion-weighted images (n=5791). Those who died during hospitalization because of an index stroke (n=158) and who had an insufficient number of BP measurements (n=119) were excluded. Local ethics committees allowed collection of data from the CRCS-K registry without individual participant informed consent as the study was deemed a quality improvement project and individual participants were not directly identified. Use of the registry database and additional collection of data, including BP metrics from the electronic medical records at the participating centers for this study, were approved by the local ethics committees at the relevant study centers.

BP and Clinical Data Collection

BP data were collected at 7 time points after onset of stroke (day 0, day 3, day 7, day 30, day 90, day 180, and day 365). BP was measured during hospitalization following institutional protocols for acute stroke management and according to routine outpatient protocols. BP measurements obtained after occurrence of study outcome events were excluded from the analysis. A total of 452 654 systolic BP (SBP) measurements were collected along with the date and time of measurement. Furthermore, SBP measurements were classified according to their closest date and time of measurement in relation to the 7 prespecified time points. The median number of time point measurements was 5 (interquartile range, 3–6). The number of patients with SBP data at each time point and the median duration from the time of the measurement to the designated time points are described in Table S1. Patients with <2 SBP time point measurements were regarded as having an insufficient number of BP measurements and were excluded from the analysis.

The following information was extracted from the stroke registry database: (1) demographics and clinical information on vascular risk factors (hypertension, diabetes, hyperlipidemia, atrial fibrillation, coronary heart disease, current smoking, and history of stroke or transient ischemia attack); (2) stroke characteristics (initial stroke severity, according to the National Institutes of Health Stroke Scale score, and categorization of stroke subtypes, according to a modified TOAST [Trial of ORG 10172 in Acute Stroke Treatment] classification system[13]); (3) time from onset of stroke to hospital

arrival time; (4) premorbid functional status, according to the modified Rankin scale; (5) symptomatic steno-occlusion (>50% of stenosis or occlusion) status of relevant major cerebral arteries; (6) acute treatment modalities; and (7) medications at discharge.

Data on administration of antihypertensive agents during hospitalization and in the outpatient follow-up period were obtained from the reimbursement claims database at each hospital. From these data, the number of antihypertensive agents and the date and duration (in days) of their administration were obtained.

Outcome Measures

The primary outcome measure was a composite of stroke recurrence, myocardial infarction, and all-cause mortality. The secondary outcome measures were stroke recurrence and all-cause mortality. All outcome events were captured prospectively up to 1 year after the index stroke, based on structured telephone interview or during routine follow-up visits at the outpatient clinics. Detailed definitions of outcomes and the protocols of the CRCS-K registry are published elsewhere.[11,12]

Statistical Analysis

We applied a group-based trajectory model approach using the TRAJ procedure of SAS software to determine the SBP trajectories during the first year after stroke and categorized patients according to the trajectory groups.[8,14] Briefly, this approach is an application of a finite mixture model, in which the longitudinal SBP data were fitted and grouped by a maximum likelihood method as a mixture of multiple latent trajectories in a censored normal model with a polynomial function of time.[15] Patients with ≥2 SBP data at the aforementioned 7 time points were eligible for the analysis. The optimal number of groups was determined using the Bayesian information criterion comparing 2×ΔBayesian information criterion between each number of groups and polynomial orders for time function (Tables S2 and S3). Each group was named according to the visual description of the SBP trajectory.

Characteristics of each SBP trajectory group were described as mean±SD for interval variables, frequency (percentage) for categorical variables, and median with interquartile range for ordinal variables, and were compared using a χ^2 test, 1-way ANOVA, or the Kruskal-Wallis test, as appropriate. The cumulative incidence of the primary and secondary outcomes in each SBP trajectory group was estimated using the Kaplan-Meier (product-limit) method and was compared using the log-rank test.

For multivariable analysis, a shared frailty model with the participating centers as a random effect was adopted along with predetermined covariates. Hazard ratios (HRs) of SBP trajectory groups for each outcome were provided by: (1) an unadjusted model; (2) model 1, adjusting for age, sex, time from onset to arrival, stroke subtype, and initial National Institutes of Health Stroke Scale score; and (3) model 2, adjusting for covariates included in model 1 and additional variables of prestroke modified Rankin scale score, hypertension, diabetes, hyperlipidemia, history of stroke or transient ischemia attack, atrial fibrillation, coronary heart disease, current smoking, intravenous thrombolysis, endovascular thrombectomy, discharge medications (antiplatelet, anticoagulant, statin, and antihypertensive agents [angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, β-blocker, calcium channel blocker, and diuretics]), and symptomatic steno-occlusion of relevant major cerebral arteries. The *moderate SBP* group was selected as a reference category, because it had the largest number of patients and its group mean was near the SBP level above which treatment is recommended according to stroke guidelines.

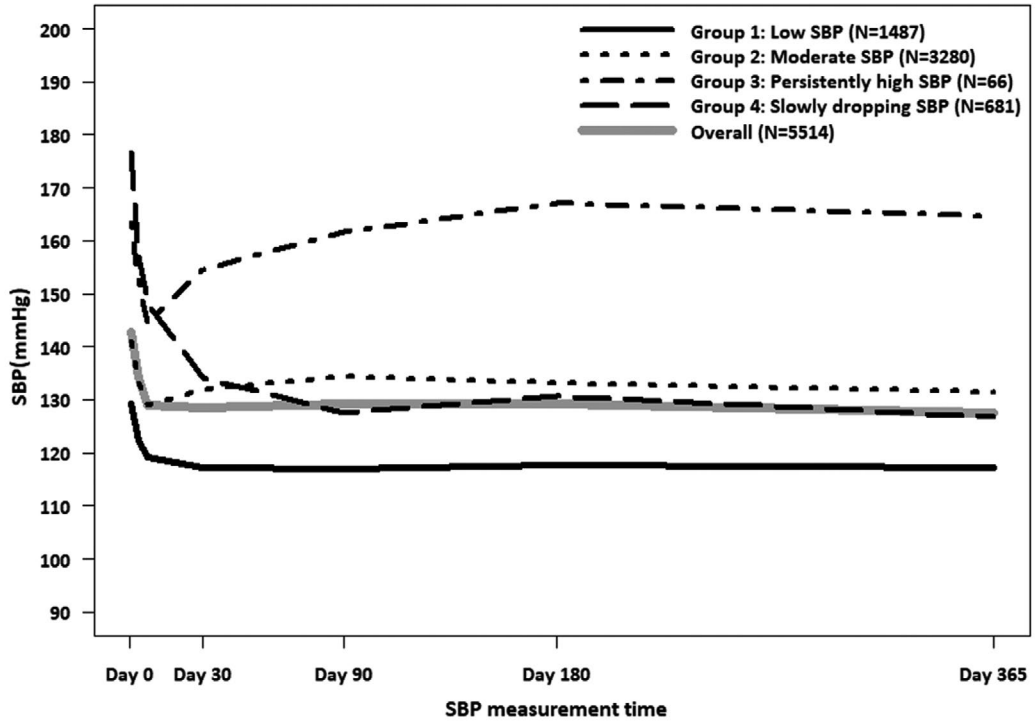
For the sensitivity analysis, the group-based trajectory modeling approach was restricted to the patients who had ≥3 and ≥4 SBP data at the 7 time points. Also, we performed an analysis that considered baseline SBP as a covariate in the model.

All statistical analyses were conducted using SAS software version 9.4 (SAS Institute Inc, Cary, NC) and R software version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria). $P<0.05$ was considered as statistically significant.

RESULTS

A total of 5514 patients (age, 67.3±12.8 years; men, 59.1%) were included in the final analysis. Using the group-based trajectory model, the patients were grouped into 4 SBP trajectory categories (Figure 1 and Table S3). On the basis of the visual depiction of the SBP curves over time, the SBP trajectory groups were named and included the following numbers of participants (parenthesis): "*low SBP*" (n=1487), "*moderate SBP*" (n=3280), "*persistently high SBP*" (n=66), and "*slowly dropping SBP*" (n=681). In the first 3 groups, SBP decreased in the first 3 to 7 days and remained steady thereafter. After the first few days of rapid BP decrement, the mean SBP in these groups was in the range of ≈114 to 116 mm Hg in the *low SBP group*, 130 to 135 mm Hg in the *moderate SBP group*, and 147 to 171 mm Hg in the *persistently high SBP group*. In the *slowly dropping SBP group*, the SBP trajectory decreased more slowly over the first month, from 182 to 135 mm Hg, and then paralleled the SBP trajectory of the *moderate SBP group*.

The patient characteristics differed among the SBP trajectory groups (Table 1). The *persistently high SBP*



	Day 0	Day 3	Day 7	Day 30	Day 90	Day 180	Day 365
Low SBP, mmHg (mean ±SD)	124.68±17.42	118.56±13.99	116.00±13.29	113.79±13.98	113.52±13.51	114.66±13.06	114.17±13.95
Moderate SBP, mmHg (mean ±SD)	142.28±18.76	134.23±16.29	130.07±15.17	132.60±16.08	135.19±15.29	133.90±14.79	131.97±15.42
Persistently high SBP, mmHg (mean ±SD)	167.77±22.83	154.53±19.93	146.65±20.27	157.92±19.70	164.67±17.24	171.02±18.96	168.51±24.34
Slowly dropping SBP, mmHg (mean ±SD)	181.70±22.10	160.41±18.89	150.49±17.34	134.98±19.07	126.73±16.24	130.42±17.01	125.92±14.95
Overall, mmHg (mean ±SD)	142.82±25.49	134.24±20.78	129.09±18.33	128.57±18.52	129.14±18.27	129.30±17.81	127.81±17.94

Figure 1. Systolic blood pressure (SBP) trajectory patterns until 1 year after index stroke event.

group was younger than the other groups and was more likely to have vascular risk factors, such as hypertension or diabetes, whereas the *low SBP group* was more likely to have atrial fibrillation (26%). Nearly 90% of individuals in the *slowly dropping SBP group* and *persistently high SBP group* had hypertension, and >70% of those in these 2 groups were on antihypertensive medications at discharge. In terms of antihypertensive drug class, renin-angiotensin-aldosterone system inhibitors were most frequently prescribed at discharge, followed by calcium channel blockers. β-Blockers or diuretics were prescribed infrequently. The proportion of individuals diagnosed with hypertension before the index stroke was markedly higher in the *slowly dropping SBP group* and in the *persistently high SBP group* than in the other 2 groups. In terms of stroke subtypes, large artery atherosclerosis was most common in the *persistently high SBP group* (59%), whereas cardioembolic stroke was most common in the *low SBP group* (30%).

The median follow-up duration was 373 (interquartile range, 363–399) days. Overall, the 1-year cumulative incidence was 11.9% for the primary outcome, 5.0% for stroke recurrence, and 8.2% for all-cause mortality. Causes of death were described in Table S4. The cumulative incidences of the 3 outcome measures in each SBP trajectory group at 5 time points (7^{th}, 30^{th}, 90^{th}, 180^{th}, and 365^{th} day) are presented in Figure 2 and Table 2. The cumulative incidence of the primary outcome was highest in the *slowly dropping SBP group* at most of the time points, but was not different between the *slowly dropping SBP group* and the *persistently high SBP group* at 1 year (15.7% versus

Table 1. Comparison of Baseline Characteristics Among SBP Trajectory Groups

Characteristic	Low SBP (n=1487)	Moderate SBP (n=3280)	Persistently high SBP (n=66)	Slowly dropping SBP (n=681)	*P* value
Age, mean±SD, y	66.04±13.55	67.96±12.45	63.00±10.78	67.31±12.43	<0.001
Men	889 (59.8)	1946 (59.3)	38 (57.6)	384 (56.4)	0.477
Body mass index, mean±SD, kg/m^2	23.14±3.25	23.72±3.09	25.67±3.31	23.91±3.27	<0.001
Onset to arrival time, median (IQR), h	7.15 (1.88–30.23)	9.42 (2.57–35.19)	21.81 (6.45–52.38)	9.00 (2.52–27.50)	<0.001
Hypertension	805 (54.1)	2444 (74.5)	59 (89.4)	602 (88.4)	<0.001
Diagnosed before hospitalization	708 (47.6)	2161 (65.9)	55 (83.3)	488 (71.7)	<0.001
On antihypertensive agents before hospitalization	636 (42.8)	1869 (57.0)	49 (74.2)	382 (56.1)	<0.001
Diagnosed after hospitalization	97 (6.5)	283 (8.6)	4 (6.1)	114 (16.7)	<0.001
Diabetes	454 (30.5)	1148 (35.0)	41 (62.1)	258 (37.9)	<0.001
Hyperlipidemia	531 (35.7)	1162 (35.4)	31 (47.0)	223 (32.7)	0.111
Atrial fibrillation	389 (26.2)	569 (17.3)	4 (6.1)	96 (14.1)	<0.001
Coronary heart disease	159 (10.7)	295 (9.0)	6 (9.1)	51 (7.5)	0.092
Stroke or TIA	338 (22.7)	792 (24.1)	22 (33.3)	147 (21.6)	0.104
Current smoker	398 (26.8)	850 (25.9)	20 (30.3)	192 (28.2)	0.547
Prestroke mRS score					0.865
0	1222 (82.2)	2696 (82.2)	51 (77.3)	560 (82.2)	
1	87 (5.9)	216 (6.6)	5 (7.6)	42 (6.2)	
≥2	178 (12.0)	368 (11.2)	10 (15.2)	79 (11.6)	
Initial NIHSS score, median (IQR)	4 (2–9)	3 (2–7)	2.5 (1–4)	4 (2–8)	<0.001
Stroke subtype					<0.001
Large artery atherosclerosis	465 (31.3)	1345 (41.0)	39 (59.1)	289 (42.4)	
Small vessel occlusion	192 (12.9)	633 (19.3)	12 (18.2)	142 (20.9)	
Cardioembolism	439 (29.5)	601 (18.3)	4 (6.1)	107 (15.7)	
Other determined	45 (3.0)	63 (1.9)	1 (1.5)	13 (1.9)	
Undetermined	346 (23.3)	638 (19.5)	10 (15.2)	130 (19.1)	
Symptomatic steno-occlusion of the relevant arteries	712 (47.9)	1508 (46.0)	34 (51.5)	312 (45.8)	0.513
Intravenous thrombolysis	225 (15.1)	361 (11.0)	2 (3.0)	75 (11.0)	<0.001
Endovascular reperfusion therapy	127 (8.5)	155 (4.7)	0 (0.0)	25 (3.7)	<0.001
Antiplatelet at discharge	1104 (74.2)	2777 (84.7)	62 (93.9)	589 (86.5)	<0.001
Anticoagulation at discharge	445 (29.9)	554 (16.9)	4 (6.1)	105 (15.4)	<0.001
Statin at discharge	1163 (78.2)	2677 (81.6)	57 (86.4)	597 (87.7)	<0.001
Antihypertensive agents at discharge	547 (36.8)	1645 (50.2)	49 (74.2)	485 (71.2)	<0.001
ACEI or ARB	345 (63.1)	1121 (68.1)	38 (77.6)	308 (63.5)	
β-Blockers	117 (21.4)	281 (17.1)	11 (22.4)	86 (17.7)	
Calcium channel blockers	212 (38.8)	769 (46.7)	27 (55.1)	317 (65.4)	
Diuretics	109 (19.9)	268 (16.3)	7 (14.3)	87 (17.9)	

Values are numbers of patients (percentages) if not otherwise indicated.

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; IQR, interquartile range; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; and TIA, transient ischemic attack.

15.8%). The cumulative incidence of all-cause mortality was highest in the *slowly dropping SBP group* at all the time points. The 1-year cumulative incidences for all outcomes in the *low SBP group* were not different statistically from those in the *moderate SBP group*, although the values were numerically higher in the *moderate SBP group* than in the *low SBP group*.

In both adjusted model 1 and model 2, the *slowly dropping SBP group* had a significantly higher risk of the primary outcome and all-cause mortality compared with the *moderate SBP group* (Table 3). But the risk of stroke recurrence was not different among SBP trajectory groups. Compared with the *moderate SBP group*, the *low SBP group* and the *persistently high*

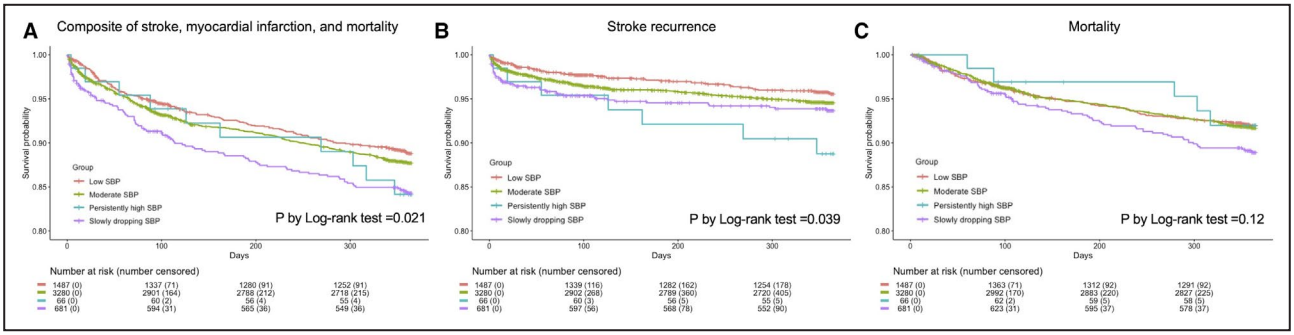


Figure 2. Kaplan-Meier survival curves for outcome events by systolic blood pressure (SBP) trajectory group.
A, Primary outcome (composite of stroke, myocardial infarction, and mortality). **B**, Stroke recurrence. **C**, Mortality.

SBP group had numerically lower and higher risk of all the outcomes, respectively, but those increased or decreased risks were not statistically significant, except for the increased risk of the composite outcome in the *persistently high SBP group* (adjusted HR, 1.93; 95% CI, 1.03–3.64). Pairwise comparison of each group also showed increased risk in the *persistently high SBP* or *slowly dropping SBP group* (Table S5).

Information on the antihypertensive drug prescription during the 1-year follow-up period was available for 3627 patients. The prescription rate of any antihypertensive agent increased to ≈70% during the first 2 months poststroke and then declined slightly (Figure S1). The prescription rate of >1 agent followed a similar pattern. It is noted that prescription rates (any and >1 agent) in the *persistently high SBP group* were not different from those in the *low SBP group* and the *moderate SBP group* at 30 days after stroke (Figure 3). Prescription rates in the *slowly dropping SBP group* were 65.9% and 47.4% at 30 days, respectively, and were higher than in the other 3 groups.

The sensitivity analysis, which was restricted to subjects who had >3 (n=4603) or >4 SBP measurements (n=3483), showed similar results for the 4 SBP trajectory groups: higher risk for the primary outcome in the *persistently high SBP group* and the *slowly dropping SBP group* and numerically lower risk in the *low SBP group* (Tables S6 through S9 and Figures S2 and S3). Another sensitivity analysis, which adjusted for baseline SBP as a covariate, also showed similar associations between SBP trajectory groups and study outcomes (Table S10).

DISCUSSION

We identified 4 distinct categories of SBP trajectory in patients with acute ischemic stroke: *low*, *moderate*, *persistently high*, and *slowly dropping SBP* groups.

Table 2. Cumulative Incidence of Outcomes, According to Time Points and SBP Trajectory Group

Variable	Day 7	Day 30	Day 90	Day 180	Day 365
Composite outcome (95% CI), %					
Low SBP	0.6 (0.2–1.0)	2.5 (1.7–3.3)	5.2 (4.1–6.4)	7.5 (6.1–8.9)	11.2 (9.5–12.8)
Moderate SBP	1.2 (0.8–1.6)	3.2 (2.6–3.8)	6.4 (5.5–7.2)	8.5 (7.5–9.5)	12.3 (11.1–13.4)
Persistently high SBP	1.5 (0.0–4.4)	3.1 (0.0–7.1)	6.1 (0.1–11.8)	9.4 (1.9–16.2)	15.8 (6.3–24.4)
Slowly dropping SBP	2.9 (1.7–4.2)	4.9 (3.2–6.5)	8.7 (6.5–10.8)	11.5 (9.0–13.9)	15.7 (12.9–18.4)
Stroke recurrence (95% CI), %					
Low SBP	0.5 (0.2–0.9)	1.4 (0.8–2.0)	2.3 (1.5–3.1)	3.0 (2.1–3.8)	4.4 (3.3–5.5)
Moderate SBP	1.1 (0.7–1.4)	2.1 (1.6–2.6)	3.4 (2.8–4.0)	4.0 (3.3–4.7)	5.4 (4.6–6.2)
Persistently high SBP	1.5 (0.0–4.4)	3.2 (0.0–7.1)	4.6 (0.0–9.5)	7.9 (1.0–14.3)	11.2 (3.0–18.8)
Slowly dropping SBP	2.5 (1.3–3.7)	3.5 (2.1–4.9)	4.6 (3.0–6.2)	5.5 (3.7–7.2)	6.3 (4.4–8.2)
Mortality (95% CI), %					
Low SBP	0.1 (0.0–0.2)	1.4 (0.8–2.0)	3.4 (2.5–4.4)	5.3 (4.1–6.5)	8.0 (6.6–9.5)
Moderate SBP	0.1 (0.0–1.2)	1.2 (0.8–1.6)	3.5 (2.8–4.1)	5.4 (4.6–6.1)	8.3 (7.4–9.3)
Persistently high SBP	0.0 (0.0–0.0)	0.0 (0.0–0.0)	3.1 (0.0–7.2)	3.1 (0.0–7.2)	8.0 (1.0–14.5)
Slowly dropping SBP	0.3 (0.0–0.7)	1.5 (0.6–2.4)	4.4 (2.8–5.9)	6.7 (4.8–8.6)	11.1 (8.6–13.4)

SBP indicates systolic blood pressure.

Table 3. Unadjusted and Adjusted HRs, According to the SBP Trajectory Groups for Outcome Events

	Unadjusted model		Adjusted model 1*		Adjusted model 2†	
Variable	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Composite outcome						
Low SBP	0.91 (0.76–1.10)	0.34	0.86 (0.71–1.04)	0.12	0.86 (0.71–1.04)	0.13
Moderate SBP	1		1		1	
Persistently high SBP	1.23 (0.65–2.30)	0.53	1.93 (1.03–3.64)	0.04	1.71 (0.90–3.23)	0.10
Slowly dropping SBP	1.30 (1.04–1.62)	0.02	1.35 (1.08–1.68)	0.009	1.32 (1.05–1.65)	0.01
Stroke recurrence						
Low SBP	0.81 (0.60–1.09)	0.16	0.77 (0.57–1.03)	0.08	0.76 (0.56–1.03)	0.07
Moderate SBP	1		1		1	
Persistently high SBP	1.85 (0.87–3.96)	0.11	2.09 (0.97–4.48)	0.06	1.74 (0.80–3.77)	0.16
Slowly dropping SBP	1.07 (0.76–1.53)	0.69	1.08 (0.76–1.54)	0.66	1.08 (0.76–1.55)	0.66
Mortality						
Low SBP	0.98 (0.78–1.22)	0.83	0.92 (0.74–1.15)	0.48	0.91 (0.73–1.14)	0.42
Moderate SBP	1		1		1	
Persistently high SBP	0.92 (0.38–2.23)	0.85	1.90 (0.78–4.62)	0.16	1.77 (0.72–4.33)	0.21
Slowly dropping SBP	1.36 (1.04–1.78)	0.02	1.40 (1.07–1.83)	0.01	1.35 (1.03–1.78)	0.03

HR (95% CI) and *P* value determined by Shared Frailty Model for considering the center effect. HR indicates hazard ratio; and SBP, systolic blood pressure.
*Adjustment for age, sex, onset to arrival time, stroke subtype, and initial National Institutes of Health Stroke Scale score.
†Adjustment for covariates included in model 1 and premorbid modified Rankin scale score, history of hypertension (diagnosed before and after admission), diabetes, hyperlipidemia, stroke or transient ischemia attack, atrial fibrillation, coronary heart disease, current smoking, intravenous thrombolysis, endovascular reperfusion therapy, discharge antiplatelet, discharge anticoagulant, discharge statin, discharge antihypertensive agent (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β-blocker, calcium channel blocker, or diuretics), and symptomatic steno-occlusion of relevant major cerebral arteries.

Longitudinal changes in the mean SBP in all the study subjects were similar to those in previous studies, in that >80% of patients with acute ischemic stroke had elevated SBP of >140 mm Hg early after ischemic stroke,[15] and the elevation of SBP was largely stabilized within 24 hours of stroke onset.[7,16] Using the BP trajectory model, we were able to identify distinguishable patterns that would not be detected by observing the overall mean of SBP. Furthermore, these patterns were associated with adverse cardiovascular outcomes.

The most noteworthy category among the 4 SBP trajectory groups was the *slowly dropping SBP group*. Compared with the *moderate SBP group*, the *slowly dropping SBP group* had markedly higher SBP (≈180 mm Hg) at stroke onset, which decreased slowly during the first month, and eventually reached a level of 120 to 130 mm Hg. At 30 days after the index stroke, SBP in the *slowly dropping SBP group* was similar to that in the *moderate SBP group*. However, the risk of the primary outcome was significantly higher in the *slowly dropping SBP group* than in the *moderate SBP group,* despite the similarity of SBP level in both groups after the first month. Furthermore, the higher risk of cardiovascular outcomes in the *slowly dropping SBP group* extended beyond the first month. This result is concordant with the findings from previous studies on BP trajectories in the acute period of stroke. For example, our prior study showed that high SBP trajectory groups based on the first 24-hour SBP measurements were at higher risk of adverse events, including mortality, up to 1 year after stroke.[8] A secondary analysis of the CATIS (China Antihypertensive Trial in Acute Ischemic Stroke) reported that the high SBP trajectory group (>160 mm Hg) based on the first 7-day SBP measurements had the highest risk of adverse events during the 2 years after stroke.[9] Interestingly, in the latter study, patients who initially had a high SBP (≈180 mm Hg), but which rapidly dropped to 140 mm Hg (within 3 days), had a lower risk of mortality than those whose SBP remained high. Our findings were similar as there was an increased risk of the primary outcome in the *persistently high SBP group*, but the result did not reach statistical significance, probably because there was a small number of patients in the group (Tables 2 and 3).

BP drop during the early stage of ischemic stroke is known to result in subsequent neurological deterioration in association with decreasing cerebral perfusion,[17] and current practice guidelines note that initiating BP-lowering therapy within the first 48 or 72 hours of onset may have no benefit.[18] However, eventually lowering SBP to guideline-based levels (eg, <140 or <130 mm Hg) in patients with stroke or transient ischemic attack is recommended to prevent subsequent cardiovascular events.[19] It is not clear when to begin lowering of BP or how quickly target BP levels should be reached in patients with acute ischemic

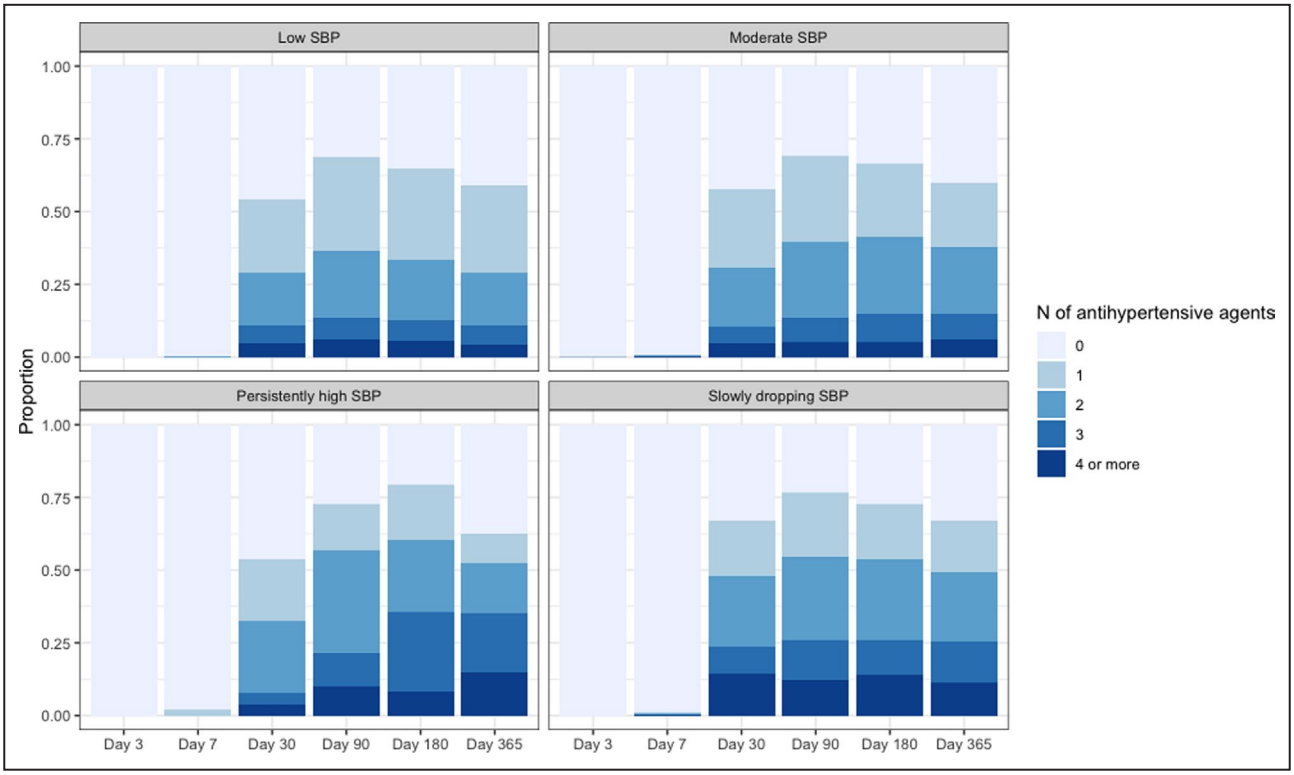


Figure 3. Number of prescribed antihypertensive agents, according to day after stroke onset, by systolic blood pressure (SBP) trajectory group.

stroke. There have been several clinical trials, such as the CATIS, ENOS (The Efficacy of Nitric Oxide in Stroke) trial, and SCAST (Scandinavian Candesartan Acute Stroke Trial), all of which failed to show a benefit of more intensive BP-lowering therapy in patients with acute stroke.[20–22] Our study results suggest that the BP trajectory immediately after the acute stage of ischemic stroke may be an important target for BP-lowering interventions. More than half of the *slowly dropping SBP group* received no antihypertensive medication or only one drug at 30 days after stroke onset (Figure 3). Intense treatment, particularly during the first 30 days after stroke onset, might improve outcomes in these patients. This area of research needs to be explored further.

It is interesting that the *slowly dropping SBP group* had worse outcomes than those in the *low SBP* or *moderate SBP group* despite the fact that the former patient group had the highest rate of multiple antihypertensive agent administration (Figure 3) and eventually reached a similar SBP level to that of the *moderate SBP group* after day 30 (Figure 1). There can be several explanations. First, there might be a clinical legacy effect whereby clinicians are afraid to lower BP acutely for concern of reducing cerebral blood flow and perfusion despite the fact that poorly controlled BP in the early period after stroke may be associated with adverse outcomes, such as neurological deterioration and poor functional outcome.[7,23] Second, elevated BP may not be the primary cause of the adverse cardiovascular outcomes. Specifically, the primary underlying causal link might be related to increased sympathetic activity, which is associated with higher stroke severity and other medical complications rather than elevated BP as the primary causal link.[24,25] Third, there might be residual confounding and some other yet unidentified factor that explains the causality.

The *low SBP group* did not have significantly better outcomes than the *moderate SBP group* (Tables 2 and 3). This result might be explained by previous observational studies that there may be a "J-shaped" association between BP and outcomes.[26,27] Our data showed that the *low SBP group* was more likely to have atrial fibrillation and coronary heart disease and to present with more severe neurologic deficits at arrival, all of which could increase mortality (Table S11).

Our study has several limitations. First, as we included patients who had SBP measurements taken at no fewer than 2 of 7 time points, there might be a potential selection bias. On the other hand, only 2 measurements may not be adequate for estimating BP trajectories. We intended to maximize the inclusion of such patients to minimize possible selection

bias and performed sensitivity analysis with subjects with ≥3 and ≥4 SBP measurements, which demonstrated the robustness of our study results. Second, although we were able to find associations between 1-year SBP trajectories and outcomes, we cannot conclude that there is a causal relationship between our main outcome findings and SBP trajectory results. However, we analyzed SBP measurements that were obtained before outcome events to maintain the temporal relationships between SBP measurements and outcome events. Third, all the centers participating in the CRCS-K registry are academic hospitals, and therefore the generalizability of the study results to the entire stroke population might be limited.

ARTICLE INFORMATION

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Supplemental Material

Appendix S1
Tables S1–S11
Figures S1–S3

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SUPPLEMENTAL MATERIAL

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Table S1. Number of patients with systolic blood pressure data allocated to each time point and distance from time points (N=5,633)

	Day 0	Day 3	Day 7	Day 30	Day 90	Day 180	Day 365
N of patients	4275	4125	4711	3360	2703	2646	2417
Distance from SBP measurement time to each timepoint (days, median (interquartile range))	0.37 (0.13-0.68)	0.05 (0.01-0.35)	0.23 (0.05-1.34)	6.25 (2.24-10.34)	12.14 (5,70-20.61)	17.13 (8.16-29.77)	19.62 (9.18–35.44)

Table S2. Interpretation of the logged Bayes factor (2×ΔBIC)

2×ΔBIC	Evidence Against H0
0 to 2	Not worth mentioning
2 to 6	Positive
6 to 10	Strong
> 10	Very strong

Table S3. Selection of number of groups for group-based trajectory model (number of blood pressure measurement ≥2 times)

		Model Fit			
Number of Groups	Polynomial	AIC	BIC	2×ΔBIC	
1	2nd order	-110334.0	-110347.2		
2	2nd order	-109616.6	-109643.0	3.15	
3	2nd order	-109468.9	-109508.6	2.43	
4	2nd order	-109356.5	-109409.4	2.30	
5	2nd order	-109336.1	-109402.2	1.16	
6	2nd order	-109306.6	-109386.0	1.51	
1	3rd order	-110204.7	-110221.2		
2	3rd order	-109385.3	-109418.4	3.21	
3	3rd order	-109162.1	-109211.7	2.62	
4	3rd order	-109047.3	-109113.4	2.29	2.77*
5	3rd order	-108988.0	-109070.7	1.93	
6	3rd order	-108957.7	-109056.9	1.44	

ΔBIC is the BIC of the alternative (more complex) model less the BIC of the null (simpler) model

2nd order= Linear + Quadratic

3rd order= Linear + Quadratic + Cubic

* Comparison with 2nd order

AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion

Table S4. Number of mortality events according to causes of death

	All-cause mortality (%)	Vascular death (%)	Stroke related death (%)	Myocardial infarction related death (%)
Total	450 (8.2)	89 (1.6)	45 (0.8)	10 (0.2)
Low SBP	114 (7.7)	25 (1.7)	12 (0.8)	1 (0.07)
Moderate SBP	259 (7.9)	53 (1.6)	28 (0.9)	7 (0.2)
Persistently high SBP	5 (7.6)	2 (3.0)	1 (1.5)	1 (1.5)
Slowly dropping SBP	72 (10.6)	9 (1.3)	4 (0.6)	1 (0.1)

* Vascular death was defined as any death during the index stroke admission, death caused by recurrent stroke, myocardial infarction or congestive heart failure, or sudden death without an identifiable nonvascular cause.

Table S5. Pairwise comparison of unadjusted and adjusted hazard ratios according to the systolic blood pressures trajectory groups for outcome events

	P-value by Log-rank test	Unadjusted model		Adjusted Model 1†		Adjusted Model 2‡	
		HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Composite outcome							
Low SBP vs. Moderate SBP	0.51	0.91 (0.76-1.10)	0.34	0.86 (0.71-1.04)	0.12	0.86 (0.71-1.04)	0.13
Persistently high SBP vs. Moderate SBP	0.57	1.23 (0.65-2.30)	0.53	1.93 (1.03-3.64)	0.04	1.71 (0.90-3.23)	0.10
Slowly dropping SBP vs. Moderate SBP	0.11	1.30 (1.04-1.62)	0.02	1.35 (1.08-1.68)	<0.01	1.32 (1.05-1.65)	0.02
Persistently high SBP vs. Low SBP	0.06	1.34 (0.71-2.55)	0.37	2.24 (1.18-4.27)	0.01	1.98 (1.03-3.80)	0.04
Slowly dropping SBP vs. Low SBP	0.005	1.42 (1.10-1.83)	0.007	1.56 (1.21-2.02)	0.0006	1.53 (1.17-1.99)	0.002
Persistently high SBP vs. Slowly dropping SBP	0.02	0.95 (0.49-1.82)	0.87	1.44 (0.75-2.77)	0.28	1.30 (0.67-2.50)	0.44
Stroke recurrence							
Low SBP vs. Moderate SBP	0.24	0.81 (0.60-1.09)	0.16	0.77 (0.57-1.03)	0.08	0.76 (0.56-1.03)	0.07
Persistently high SBP vs. Moderate SBP	0.94	1.85 (0.87-3.96)	0.11	2.09 (0.97-4.48)	0.06	1.74 (0.80-3.77)	0.16
Slowly dropping SBP vs. Moderate SBP	0.71	1.07 (0.76-1.53)	0.69	1.08 (0.76-1.54)	0.66	1.08 (0.76-1.55)	0.66
Persistently high SBP vs. Low SBP	0.02	2.29 (1.04-5.02)	0.04	2.72 (1.23-6.02)	0.01	2.30 (1.02-5.17)	0.04
Slowly dropping SBP vs. Low SBP	0.03	1.32 (0.88-1.99)	0.18	1.41 (0.93-2.13)	0.10	1.43 (0.93-2.20)	0.10
Persistently high SBP vs. Slowly dropping SBP	0.52	1.73 (0.77-3.87)	0.18	1.93 (0.86-4.35)	0.11	1.61 (0.71-3.63)	0.26

Mortality							
Low SBP vs. Moderate SBP	0.96	0.98 (0.78-1.22)	0.83	0.92 (0.74-1.15)	0.48	0.91 (0.73-1.14)	0.42
Persistently high SBP vs. Moderate SBP	0.46	0.92 (0.38-2.23)	0.85	1.90 (0.78-4.62)	0.16	1.77 (0.72-4.33)	0.21
Slowly dropping SBP vs. Moderate SBP	0.09	1.36 (1.04-1.78)	0.02	1.40 (1.07-1.83)	0.01	1.35 (1.03-1.78)	0.03
Persistently high SBP vs. Low SBP	0.47	0.94 (0.38-2.31)	0.89	2.05 (0.83-5.06)	0.12	1.94 (0.78-4.82)	0.15
Slowly dropping SBP vs. Low SBP	0.06	1.40 (1.03-1.89)	0.03	1.52 (1.12-2.06)	0.007	1.49 (1.08-2.04)	0.01
Persistently high SBP vs. Slowly dropping SBP	0.02	0.67 (0.27-1.67)	0.40	1.35 (0.54-3.37)	0.52	1.31 (0.52-3.28)	0.57

HRs were estimated for the former group with the latter group as a reference.

† Adjustment for age, sex, onset to arrival time, stroke subtype, and initial National Institute of Health Stroke Scale score

‡ Adjustment for covariates included in Model 1 and premorbid modified Rankin's scale score, history of hypertension (diagnosed before and after admission), diabetes, hyperlipidemia, stroke or transient ischemia attack, atrial fibrillation, coronary heart disease, current smoking, intravenous thrombolysis, endovascular reperfusion therapy, discharge antiplatelet, discharge anticoagulant, discharge statin, discharge antihypertensive agent (angiotensin converting enzyme inhibitors or angiotensin receptor blockers, beta-blocker, calcium channel blocker, diuretics), and symptomatic steno-occlusion of relevant major cerebral arteries

HR (95%CI) and P-value by Shared Frailty Model for considering the center effect

HR, hazard ratio; CI, confidence interval;
SBP, systolic blood pressure

Table S6. Selection of number of groups for group-based trajectory model (number of blood pressure measurement ≥3 times) (N = 4,603)

		Model Fit			
Number of Groups	Polynomial	AIC	BIC	2×ΔBIC	
1	2nd order	-102239.5	-102252.4		
2	2nd order	-101563.9	-101589.7	3.12	
3	2nd order	-101419.0	-101457.6	2.42	
4	2nd order	-101305.6	-101357.1	2.30	
5	2nd order	-101284.2	-101348.6	1.23	
6	2nd order	-101257.4	-101334.6	1.45	
1	3rd order	-102115.9	-102132.0		
2	3rd order	-101350.3	-101382.4	3.18	
3	3rd order	-101130.8	-101179.0	2.61	
4	3rd order	-101015.0	-101079.4	2.30	2.74*
5	3rd order	-100960.2	-101040.7	1.89	
6	3rd order	-100928.1	-101024.6	1.51	

ΔBIC is the BIC of the alternative (more complex) model less the BIC of the null (simpler) model

2nd order= Linear + Quadratic

3rd order= Linear + Quadratic + Cubic

* Comparison with 2nd order

AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion

Table S7. Unadjusted and adjusted hazard ratios according the SBP trajectory groups for outcome events (number of blood pressure measurement ≥3 times, N = 4,603)

	Unadjusted Model		Adjusted Model 1†		Adjusted Model 2‡	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Composite outcome						
Low SBP	0.94 (0.76-1.17)	0.59	0.84 (0.68-1.05)	0.13	0.86 (0.69-1.08)	0.19
Moderate SBP	1		1		1	
Persistently high SBP	1.33 (0.71-2.50)	0.38	2.02 (1.07-3.81)	0.03	1.71 (0.90-3.24)	0.10
Slowly dropping SBP	1.21 (0.94-1.55)	0.14	1.30 (1.01-1.66)	0.04	1.28 (1.00-1.65)	0.053
Stroke recurrence						
Low SBP	0.79 (0.56-1.10)	0.17	0.72 (0.51-1.02)	0.06	0.72 (0.51-1.02)	0.07
Moderate SBP	1		1		1	
Persistently high SBP	1.91 (0.89-4.10)	0.19	2.10 (0.98-4.53)	0.06	1.69 (0.78-3.69)	0.19
Slowly dropping SBP	1.02 (0.70-1.49)	0.90	1.03 (0.71-1.51)	0.86	1.04 (0.70-1.53)	0.85
Mortality						
Low SBP	1.02 (0.79-1.34)	0.86	0.91 (0.69-1.18)	0.47	0.92 (0.70-1.21)	0.56
Moderate SBP	1		1		1	
Persistently high SBP	1.07 (0.44-2.61)	0.88	2.17 (0.88-5.32)	0.09	1.94 (0.78-4.78)	0.15
Slowly dropping SBP	1.27 (0.93-1.73)	0.13	1.37 (1.01-1.86)	0.046	1.33 (0.97-1.82)	0.08

† Adjusted for age, sex, onset to arrival time, stroke subtype, and initial National Institute of Health Stroke Scale score

‡ Adjusted for covariates for model 2 and premorbid modified Rankin's scale score, history of hypertension (diagnosed before and after admission), diabetes, hyperlipidemia, stroke or transient ischemia attack, atrial fibrillation, coronary heart disease, current smoking, intravenous thrombolysis, endovascular reperfusion therapy, discharge antiplatelet, discharge anticoagulant, discharge statin, discharge antihypertensive agent (Angiotensin converting enzyme inhibitors or Angiotensin receptor blockers, beta blocker, calcium channel blocker, diuretics), and symptomatic steno-occlusion of relevant artery

HR (95% CI) and P-value by Shared Frailty Model for considering the center effect

HR, hazard ratio; CI, confidence interval; SBP, systolic blood pressure

Table S8. Selection of number of groups for group-based trajectory model (number of blood pressure measurement ≥4 times) (N = 3,483)

		Model Fit			
Number of Groups	Polynomial	AIC	BIC	2×ΔBIC	
1	2nd order	-87190.7	-87203.1		
2	2nd order	-86590.9	-86615.5	3.07	
3	2nd order	-86445.6	-86482.6	2.42	
4	2nd order	-86327.2	-86376.4	2.33	
5	2nd order	-86302.1	-86363.7	1.41	
6	2nd order	-86274.5	-86348.4	1.49	
1	3rd order	-87081.6	-87097.0		
2	3rd order	-86403.5	-86434.3	3.12	
3	3rd order	-86182.1	-86228.3	2.61	
4	3rd order	-86064.5	-86126.1	2.31	2.74*
5	3rd order	-86007.3	-86084.2	1.92	
6	3rd order	-85971.9	-86064.3	1.60	

ΔBIC is the BIC of the alternative (more complex) model less the BIC of the null (simpler) model

2nd order= Linear + Quadratic

3rd order= Linear + Quadratic + Cubic

* Comparison with 2nd order

AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion

Table S9. Unadjusted and adjusted hazard ratios according the SBP trajectory groups for outcome events (number of blood pressure measurement ≥4 times, N = 3,483)

	Unadjusted Model		Adjusted Model 1†		Adjusted Model 2‡	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Composite outcome						
Low SBP	1.26 (0.95-1.68)	0.11	1.10 (0.83-1.47)	0.50	1.12 (0.84-1.51)	0.44
Moderate SBP	1		1		1	
Persistently high SBP	2.02 (1.03-3.98)	0.04	2.43 (1.23-4.80)	0.01	1.86 (0.93-3.73)	0.08
Slowly dropping SBP	1.31 (0.95-1.80)	0.10	1.38 (1.00-1.89)	0.0497	1.42 (1.02-1.96)	0.04
Stroke recurrence						
Low SBP	0.94 (0.64-1.38)	0.74	0.86 (0.58-1.28)	0.47	0.85 (0.57-1.28)	0.44
Moderate SBP	1		1		1	
Persistently high SBP	2.34 (1.08-5.06)	0.03	2.43 (1.12-5.30)	0.03	1.81 (0.81-4.05)	0.15
Slowly dropping SBP	0.97 (0.63-1.50)	0.89	0.97 (0.63-1.50)	0.90	0.96 (0.61-1.51)	0.86
Mortality						
Low SBP	1.56 (1.06-2.30)	0.02	1.34 (0.91-2.00)	0.14	1.38 (0.92-2.06)	0.12
Moderate SBP	1		1		1	
Persistently high SBP	2.04 (0.74-5.61)	0.17	3.07 (1.10-8.53)	0.03	2.53 (0.90-7.10)	0.08
Slowly dropping SBP	1.57 (1.02-2.42)	0.04	1.72 (1.12-2.65)	0.01	1.88 (1.21-2.91)	0.005

† Adjusted for age, sex, onset to arrival time, stroke subtype, and initial National Institute of Health Stroke Scale score

‡ Adjusted for covariates for model 2 and premorbid modified Rankin's scale score, history of hypertension (diagnosed before and after admission), diabetes, hyperlipidemia, stroke or transient ischemia attack, atrial fibrillation, coronary heart disease, current smoking, intravenous thrombolysis, endovascular reperfusion therapy, discharge antiplatelet, discharge anticoagulant, discharge statin, discharge antihypertensive agent (Angiotensin converting enzyme inhibitors or Angiotensin receptor blockers, beta blocker, calcium channel blocker, diuretics), and symptomatic steno-occlusion of relevant artery

HR (95% CI) and P-value by Shared Frailty Model for considering the center effect

HR, hazard ratio; CI, confidence interval; SBP, systolic blood pressure

Table S10. Adjusted hazard ratios according to the systolic blood pressures trajectory groups for outcome events, further adjusted by baseline systolic blood pressure (N = 5,514)

	Adjusted Model†	
	HR (95% CI)	P-value
Composite outcome		
Low SBP	0.85 (0.70-1.03)	0.10
Moderate SBP	1	
Persistently high SBP	1.74 (0.92-3.28)	0.09
Slowly dropping SBP	1.36 (1.07-1.73)	0.01
Stroke recurrence		
Low SBP	0.77 (0.56-1.05)	0.10
Moderate SBP	1	
Persistently high SBP	1.70 (0.78-3.70)	0.18
Slowly dropping SBP	1.05 (0.72-1.53)	0.80
Mortality		
Low SBP	0.88 (0.69-1.11)	0.27
Moderate SBP	1	
Persistently high SBP	1.81 (0.74-4.44)	0.19
Slowly dropping SBP	1.44 (1.08-1.92)	0.01

† Adjustment for age, sex, onset to arrival time, stroke subtype, and initial National Institute of Health Stroke Scale score, premorbid modified Rankin's scale score, history of hypertension (diagnosed before and after admission), diabetes, hyperlipidemia, stroke or transient ischemia attack, atrial fibrillation, coronary heart disease, current smoking, intravenous thrombolysis, endovascular reperfusion therapy, discharge antiplatelet, discharge anticoagulant, discharge statin, discharge antihypertensive agent (angiotensin converting enzyme inhibitors or angiotensin receptor blockers, beta-blocker, calcium channel blocker, diuretics), and symptomatic steno-occlusion of relevant major cerebral arteries and baseline systolic blood pressure

HR (95% CI) and P-value by Shared Frailty Model for considering the center effect

HR, hazard ratio; CI, confidence interval; SBP, systolic blood pressure

Table S11. Comparison of baseline characteristics between patients with and without atrial fibrillation in the Low systolic blood pressure group

	Without atrial fibrillation (N=1,098)	With atrial fibrillation (N=389)	P-value
Age, mean±SD	64.35±14.17	70.82±10.22	<0.001
Male	690 (62.8)	199 (51.2)	<0.001
Body-mass index, mean±SD	23.18±3.16	23.04±3.50	0.499
Onset to arrival time, hour, median (IQR)	10.03 (2.45-39.04)	3.28 (1.18-9.83)	<0.001
Hypertension	557 (50.7)	248 (63.8)	<0.001
Diagnosed before hospitalization	484 (44.1)	224 (57.6)	<0.001
On antihypertensive agents before hospitalization	427 (38.9)	209 (53.7)	<0.001
Diagnosed after hospitalization	73 (6.6)	24 (6.2)	0.742
Diabetes	357 (32.5)	97 (24.9)	0.006
Hyperlipidemia	394 (35.9)	137 (35.2)	0.814
Coronary heart disease	107 (9.7)	52 (13.4)	0.047
Stroke or TIA	239 (21.8)	99 (25.4)	0.136
Current smoker	341 (31.1)	57 (14.7)	<0.001
Premorbid mRS score			0.896
0	904 (82.3)	318 (81.7)	
1	65 (5.9)	22 (5.7)	
2 or more	129 (11.7)	49 (12.6)	
Initial NIHSS score, median (IQR)	4 (1-7)	6 (2-13)	<0.001
Symptomatic steno-occlusion of the relevant arteries	489 (44.5)	223 (57.3)	<0.001
Intravenous thrombolysis	135 (12.3)	90 (23.1)	<0.001
Endovascular reperfusion therapy	64 (5.8)	63 (16.2)	<0.001
Antiplatelet at discharge	972 (88.5)	132 (33.9)	<0.001
Anticoagulation at discharge	137 (12.5)	308 (79.2)	<0.001
Statin at discharge	873 (79.5)	290 (74.6)	0.042
Antihypertensive agents at discharge	369 (33.6)	178 (45.8)	<0.001
ACEI or ARB	254 (68.8)	91 (51.1)	
Beta blockers	46 (12.5)	71 (39.9)	
Calcium channel blockers	159 (43.1)	53 (29.8)	
Diuretics	65 (17.6)	44 (24.7)	

Values are numbers of patients (%) if not otherwise indicated.
SD, standard deviation; IQR, interquartile range; TIA, transient ischemic attack; NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin scale; ACEI, Angiotensin converting enzyme inhibitors; ARB, Angiotensin receptor blockers

Figure S1. Number of prescribed antihypertensive agents according to day after stroke onset.

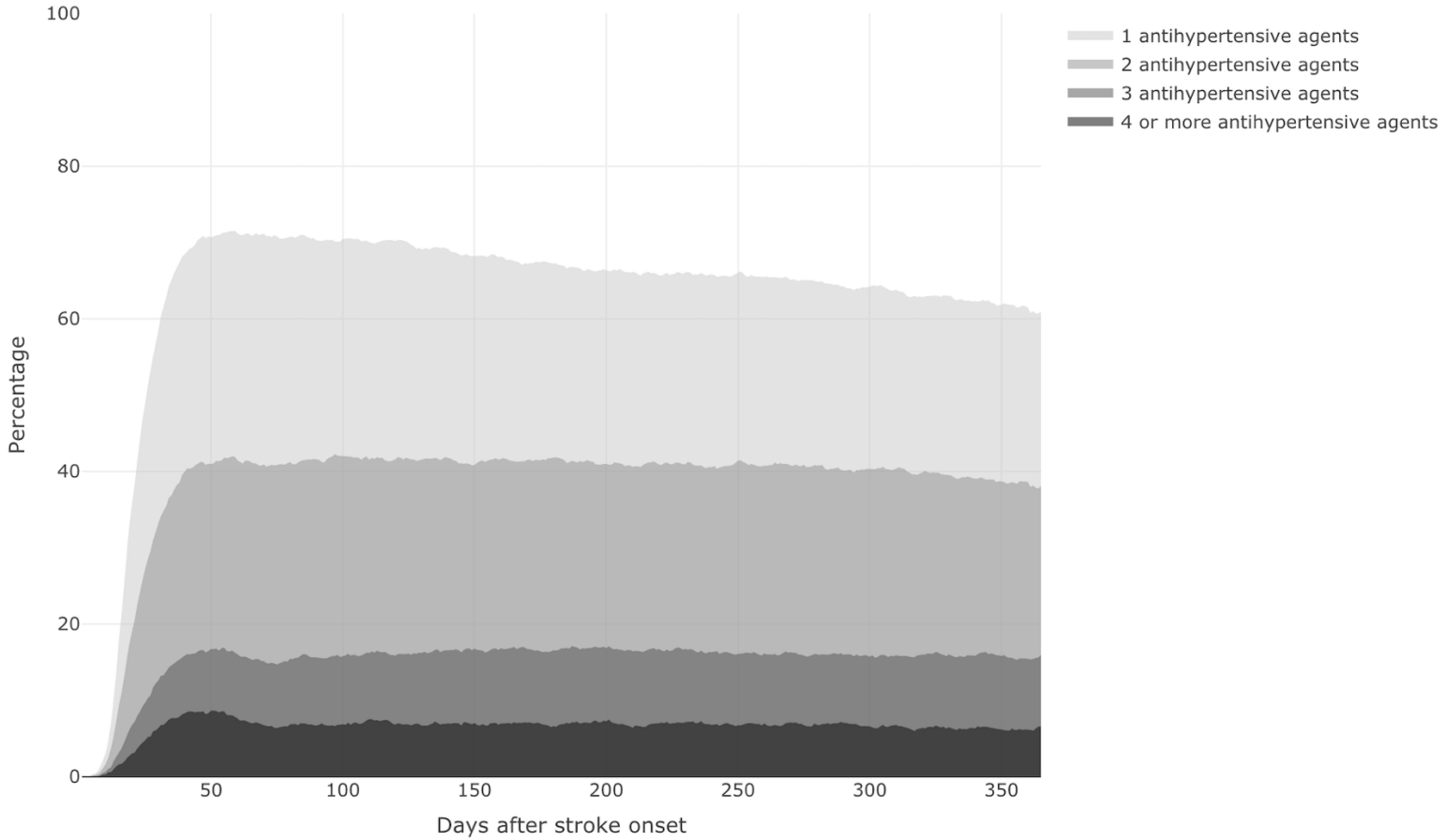
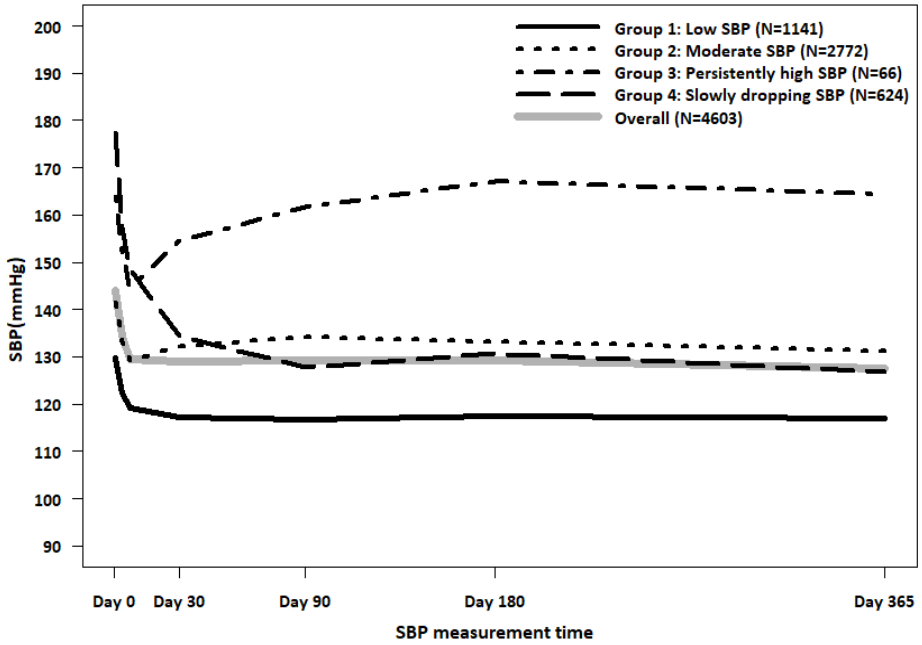
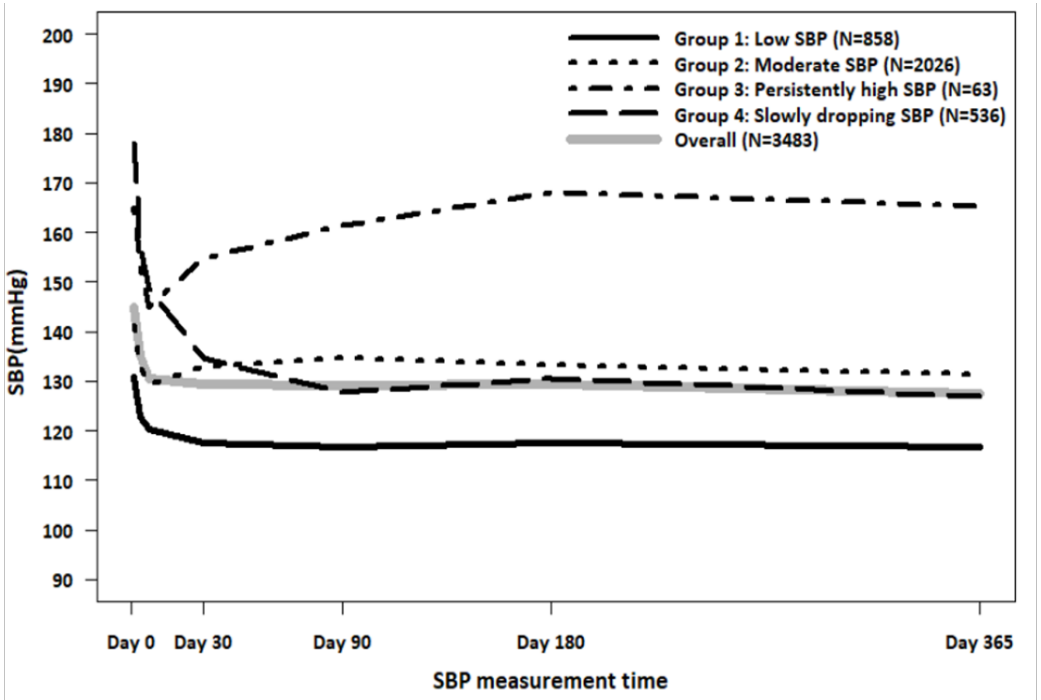


Figure S2. Systolic blood pressure trajectory patterns until 1 year after index stroke event (number of blood pressure measurement ≥ 3 times) (N = 4,603).



	Day 0	Day 3	Day 7	Day 30	Day 90	Day 180	Day 365
Low SBP, mmHg (N=1,141)	126.14±18.14	118.62±14.22	116.21±13.57	113.96±14.36	113.30±13.53	114.42±13.10	113.99±14.03
Moderate SBP, mmHg (N=2,772)	142.14±19.31	133.79±16.30	129.85±15.04	132.67±16.15	134.95±15.33	133.73±14.80	131.82±15.41
Persistently high SBP, mmHg (N=66)	167.77±22.83	154.53±19.93	146.65±20.27	157.92±19.70	164.67±17.24	171.02±18.96	168.51±24.34
Slowly dropping SBP, mmHg (N=624)	181.56±22.59	159.89±18.58	150.58±17.43	135.01±19.15	127.03±16.41	130.39±17.02	125.96±14.93
Total, mmHg (N=4,603)	143.92±25.88	134.51±20.76	129.56±18.40	128.89±18.62	129.16±18.28	129.30±17.82	127.43±17.93

Figure S3. Systolic blood pressure trajectory patterns until 1 year after index stroke event (number of blood pressure measurement ≥ 4 times) (N = 3,483).



	Day 0	Day 3	Day 7	Day 30	Day 90	Day 180	Day 365
Low SBP, mmHg (N=858)	128.4±18.9	120.3±14.9	118.3±14.2	114.5±14.4	113.4±13.2	114.6±13.1	113.9±14.0
Moderate SBP, mmHg (N=2026)	141.3±19.6	133.3±16.4	129.8±14.9	133.3±16.1	135.4±15.2	133.8±14.7	132.0±15.2
Persistently high SBP, mmHg (N=63)	167.4±23.3	153.9±19.2	146.9±20.3	157.9±19.7	164.1±17.6	171.0±19.0	168.5±24.3
Slowly dropping SBP, mmHg (N=536)	181.4±23.0	159.4±18.3	150.6±17.4	135.1±18.9	127.1±16.2	130.6±16.9	126.1±14.8
Total, mmHg (N=3,483)	144.9±26.5	135.2±20.9	130.5±18.4	129.4±18.7	129.1±18.2	129.3±17.8	127.4±17.9