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REVIEW

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Systolic blood pressure trajectories after acute ischemic strokes and clinical outcomes: A systematic review

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Abstract

Blood pressure(BP) varies drastically during the acute phase after stroke onset. BP level and BP variability may have a major impact on acute ischemic stroke (AIS) prognosis. However, the association between trajectories of blood pressure over time and clinical outcomes have not been established. This review sought out existing evidences for associations of systolic blood pressure (SBP) trajectories on outcomes after stroke to determine the connection between SBP trajectories and stroke prognosis. According to a pre-designed search strategy, literature search was carried out in Embase, Pubmed and Web of Science. Two authors independently evaluated study eligibility and quality, and literature data were extracted. When the literature was eligible, we perform meta-analysis to determine associations of SBP trajectories with clinical outcomes. Seven studies were finally screened out of 52 studies retrieved. Seven studies received a good risk of bias rating and reported BP measurement methods and intervals, BP trajectories modeling methods, outcome measures, but it was found that final systolic BP trajectories in various papers were significantly different. All studies reported statistically significant associations between systolic blood pressure trajectories and prognosis. Methodological heterogeneity is observed in studies. However, this systematic review suggests that the high SBP group after AIS is related to poor clinical outcomes, while the rapid decline or medium-to-low or low SBP group is associated with relatively better clinical outcomes at different period after stroke. More prospective studies are needed to report the full methodology according to standardized criteria and explore relationships between SBP trajectories and prognosis of stroke.

KEYWORDS
acute ischemic strokes, clinical outcomes, systematic review, systolic blood pressure trajectories

1 | INTRODUCTION

Blood pressure(BP) change widely after ischemic stroke onset. It usually increases sharply at the beginning of stroke, then gradually decreases and stabilizes within about a week in most stroke patients,[1] which is associated with poor outcomes.[2,3] Tikhonoff V' study showed that the prognosis of acute ischemic stroke (AIS) patients had a U-shaped relationship with blood pressure, and the prognosis was best when the systolic blood pressure (SBP) was about 140–180 mmHg.[4] Exorbitantly high or excessively low BP are related with poor outcomes in stroke patients.[5,6] In addition, a study has shown that the relationship between blood pressure and prognosis may depend on the time after stroke.[7] Blood pressure variability (BPV) refers to the degree of BP fluctuation within a certain period of time. Most studies suggest that high BPV after stroke is related to poor prognosis.[8,9]

In the past, blood pressure value at a time point or blood pressure variability over a period of time were used as prognostic factors. In fact, the direction and magnitude of BPV may affect prognosis.[1] Different BP change trajectories after stroke may lead to different clinical outcomes. There are few studies focus on the relationship between systolic blood pressure trajectories and stoke outcomes. There is no systematic review of the influence of SBP trajectories on clinical outcomes after AIS. This systematic review tries to resolve this question by examining the available proof on the effect of SBP trajectories on outcomes after stroke. This review was reported according to the preferred reporting items of the Systematic Evaluation and Meta-analysis (PRISMA) guidelines.[10]

2 | METHODS

2.1 | Search strategy and selection criteria

Following a pre-designed study protocol, two researchers search independently related literature in Embase, Pubmed, and Web of Science. Search terms were subject terms and sub-subject terms or synonym for blood pressure, trajectory, ischemic stroke and prognosis (Figure 1). The "AND" operator is used between search terms, and the "OR" operator is used between subject terms and sub-subject terms or synonyms. Detailed search methods were displayed in Supplementary material. The searches were limited to March 2022 and the last modified searches were in March 2022. Search results are exported electronically into EndNote for repeat identification and removal of references. According to the pre-designed eligibility criteria, we reviewed titles and abstracts of remaining references and obtained full texts of qualified studies. The references of selected studies were manual searched for additional relevant articles. Inclusion criteria: 1. AIS. 2. Report systolic blood pressure trajectories or other indicators similar to SBP trajectories, indicating the direction and amplitude of BP fluctuations (blood pressure fluctuation pattern). 3. Stroke outcomes were followed up. 4. Observational studies. Exclusion criteria: 1. Non-English language studies. 2. Unpublished studies. 3. Unavailable full-text. Study quality and risk of bias were assessed using an adapted checklist of meta-analyses of observational studies (Table S1). Any inconsistencies were reassessed by a third author and then resolved together with the other two authors.

2.2 | Data extraction

Data extraction was accomplished by two independent researchers according to a pre-designed method. The data include: Study population characteristics, classification of stroke, treatment of stroke, BP measurement device, interval and frequency, BP parameter (blood pressure trajectory modeling and groups), results of evaluation (outcome indicators and follow-up time), correlation estimation (odd ratio (OR) and 95% confidence interval (CI)), key conclusion. Relevant missing information is requested by emailing the corresponding author.

2.3 | Statistical analysis

Considering the potential heterogeneity of included studies, we discreetly decided whether a meta-analysis was appropriate. Basing on study population, systolic blood pressure groups, outcome indicators, follow-up time and so on, we determined minimum acceptable criteria for studies to be meta-analyzed: same blood pressure measurement interval and frequency, SBP groups, follow-up interval and outcome assessment, meta-analysis excluded if these criteria were not met. A meaningful result is unlikely to be observed in a meta-analysis due to the inconsistency of these factors, standardized parameters are needed for a meta-analysis to produce valuable results in the future.

3 | RESULTS

Through literature search and selection, a total of seven observational studies were included. Four prospective studies,[1,11,13,15] two retrospective studies of randomized controlled study data,[14,16] and one study involving prospective data of five centers and retrospective stroke data from four centers.[12] Six studies collected national multi-center stroke data,[1,12–16] and only one study was a single-center study.[11] Two studies respectively explored prognostic significance of systolic BP trajectories after intravenous thrombolytic (IVT) and endovascular thrombolytic (EVT).[11,12] Seven studies had good quality and risk of bias (Table S2). In these studies, study population, BP measurements, systolic blood pressure groups, outcomes evaluation, and associations between SBP trajectories and outcomes were reported, but these were not exactly the same. Most importantly, the evaluation time of SBP trajectories and stroke outcome indicators were different in the study, so included studies were of poor homogeneity and obvious heterogeneity. Therefore, meta-analysis is difficult to be performed, a descriptive analysis of these studies was conducted. Major findings from the above-mentioned data are emphasized below.

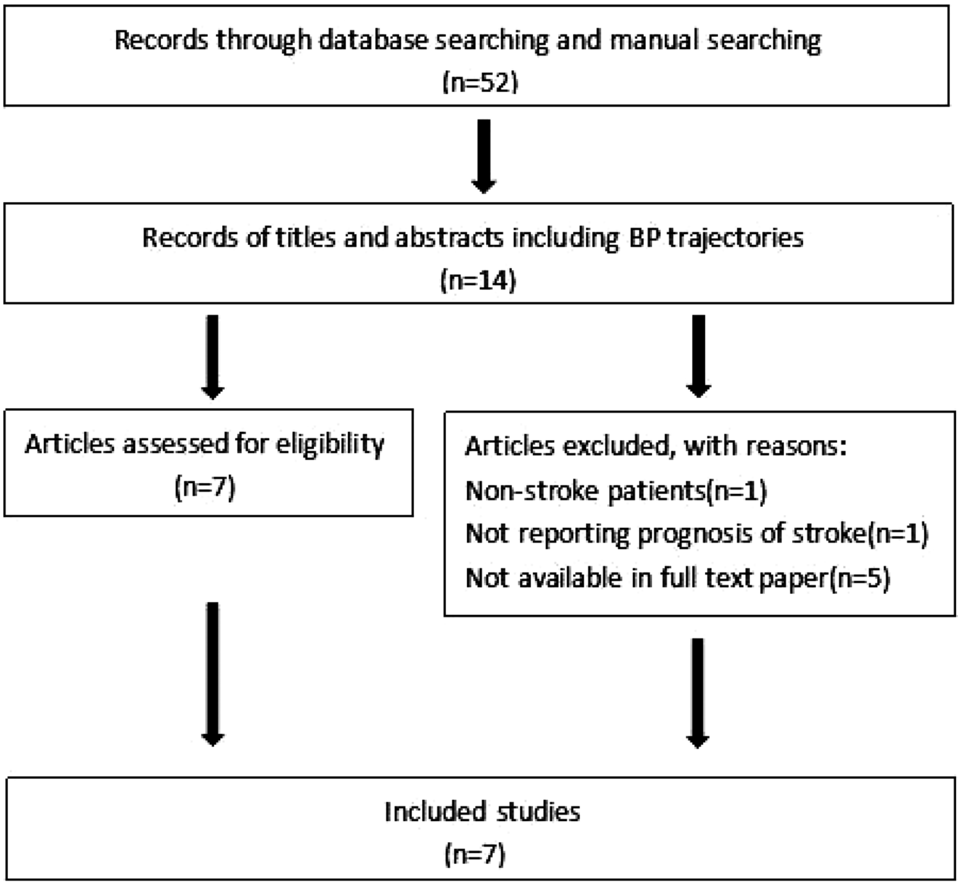

FIGURE 1 Study selection process

3.1 | Study population and baseline characteristics

The study population included AIS patients: (1) Treated with IVT within 4.5 h after stroke[11]; (2) Treated with EVT[12]; (3) Hospitalized within 24 h after stroke[1,13,15]; (4) Admitted within 48 h of onset with admission SBP between 140 and 220 mmHg.[14,16] Five studies reported treatment and intervention plans.[11,12,14–16] Most of the treatment plans were based on the latest AIS treatment guidelines and were decided by physicians in charge. Only one study classified stroke patients by TOSAT criteria.[13] All studies collected baseline characteristics of the study population, including gender, age, past medical history, alcohol and tobacco history, etc. Almost all studies suggest different clinical features in different systolic blood pressure groups. From these studies it can be observed that patients with higher BP had a higher rate of hypertension and antihypertensive medications, while those with lower BP tended to be younger.[1,11–16] At the same time, a few studies suggest patients with higher blood pressure may have a higher rate of atrial fibrillation, diabetes, hyperlipidemia[12] and have a higher body mass index(BMI) and baseline national institutes of health stroke scale (NHISS).[14] Two studies reported older age and higher NHISS scores were significantly associated with a higher risk of adverse outcomes (modified Rankin Scale score ≥3) at 3 months after stroke.[1,13] Furthermore, diabetes history and stroke type may also be predictive factors of poor prognosis.[1] The remaining five studies did not report other predictors of stroke outcome (Table 1).

3.2 | Blood pressure measurement

Blood pressure measurement was described in seven studies, two studies used a standard mercury sphygmomanometer,[14,16] two studies measured BP with a semi-automatic BP monitor,[1,13] and two studies chose non-invasive BP but did not specify measuring devices,[12,15] one study used an electrocardiogram monitor(Intelli Vue MP70; Phillips Healthcare, Franklin, TN) to obtain supine blood pressure in patients.[11]

3.3 | Blood pressure measurement interval

Seven studies reported the frequency and interval of blood pressure measurement. One study used post-discharge BP data: BP value at 14 days or discharge, 3 months, and 12 months after stroke.[16] Two studies collected BP data over a 24-h period, one study monitored blood pressure every 3 h within 24 h of admission,[15] while the other measured BP every 15 min in the first 2 h, every 30 min in the next 6 h, and every hour in the remaining 16 h after thrombolytic.[11] Three studies selected In-hospital blood pressure data, in one of which BP measurement was at

TABLE 1 Study characteristics

Study	Numbers	Study design	Population	Reperfusion therapy?	Recruitment time	BP monitoring duration	Number of trajectories	Outcome measures
Petersen NH et al. 2022	1791	observational cohort study	AIS	EVT	Not given	3 days	5	mRS score at 3 months
Fan K et al. 2021	353	Prospective study	AIS	IVT	≤4.5 h	24 hours	5	mRS score at 3 months
Xu J et al. 2019	316	Prospective cohort study	AIS	NO	≤24 h	7 days	3	mRS score at 3 months
Changwei Li et al. 2018	4016	Retrospective study	AIS	NO	≤48 h	7 days	5	mRS score at 3 and 24 months
Jie Xu et al.2019	1095	Retrospective study	AIS	NO	≤24 h	7 days	5	mRS score at 3 months
Kim BJ et al. 2018	8376	Prospective study	AIS	NO	≤24 h	24 hours	5	composite event* at 12 ± 2 months
Zheng et al. 2021	3479	Retrospective study	AIS	NO	≤48 h	1 year	4	mRS score during 12 to 24 months

*A composite of recurrent stroke, myocardial infarction and all-cause death

baseline, every 2 h for 24 h, every 4 h for 2–3 days, and every 8 h thereafter until discharge,[14] the other two papers measured BP twice a day during hospitalization (6–9 in the morning and 6–9 in the evening), and the blood pressure at admission, discharge, and 3 months was recorded at the same time.[1,13] One study recorded BP data over a 72-h period, with BP measurements taken every 2 h for the first 12 h, every 4 h for 12–24 h, and every 6 h for 24–72 h after EVT.[12]

3.4 | Systolic blood pressure trajectory groups

Two studies adopted a group-based trajectory modeling (GBTM) approach using the traj procedure in SAS to identify systolic blood pressure trajectories within 24 hours of stroke onset, and identified five SBP groups.[11,15] Three studies used latent variable mixture modeling implemented by SAS proc traj procedure to generate SBP subgroup that share a similar underlying trajectory of systolic blood pressure, two studies identified five SBP groups[12,14] and one study identified four SBP groups.[16] A random-effects mixed model by SAS Proc MIXED was used to estimated growth curve parameters of SBP and the patients were finally classified into three SBP groups.[13] One study defined BP fluctuation patterns based on the BP value in three time periods (days 1, 2, and 3–7) and determined five classes.[1] All studies identified systolic blood pressure groups based on BP level and direction and degree of change in BP over time. All the SBP groups in each study can be seen in Table 2.

3.5 | Outcome assessment

Most studies used modified Rankin Scale (mRS) score to assess stroke outcomes. Scores on the mRS ranged from 0 to 6, with a score of 0–2 indicating favorable functional outcome; a score of 3–5 indicating severe disability; and a score of six indicating death.[12,14] Four studies used mRS score of 3–6 at 3 months as the major outcome.[1,11–13] And other two papers respectively used mRS score of 3–6 during 12–24 months and at 3 and 24 months were the major outcome.[14,16] A composite of recurrent stroke, myocardial infarction, and all-cause death at about 1 year after stroke were the primary outcomes.[15]

3.6 | Systolic blood pressure trajectory groups and clinical outcomes

Studies have shown that blood pressure of AIS patients behaves in different trajectories, and these trajectories have a certain correlation with clinical prognosis. In the study of the relationship between 24 h SBP trajectories after stroke and recurrent vascular events, both an acutely elevated SBP group and a persistently high SBP group had an increased risk of having the composite events (a composite of recurrent stroke, myocardial infarction and all-cause death).[15] In patients with stroke treated with IVT, there was a U-shaped relationship between 24 h SBP trajectories and adverse outcome at 90 days. The Slow drop-low SBP group and Continuous fluctuation-very high SBP group increased the risk of adverse outcomes.[11] As for the prognostic significance of systolic blood pressure trajectories in the acute phase, the sustained high SBP group tended to have a higher rate of adverse outcomes at 3 months, other patients were divided into different SBP groups according to the degree of systolic blood pressure decline. It can be found that the lower the overall BP, the lower the adverse outcome rate in these trajectory groups (Figure 2). The risk of adverse outcomes was reduced in the rapid decline, moderate-to-low, and low SBP groups compared with the persistently high SBP group.[1,13,14] Patients treated with EVT with moderate-to-high, high-to-moderate, high SBP had an increased risk of poor outcome at 90 days.[12] After discharge, compared with the high-stability group, patients with high-decreasing and low-stable SBP had a reduced risk of adverse outcomes in two-year follow-up.[16] Key findings were shown in the Figure 2, Tables S2 and S3. To sum up, it can

TABLE 2 Systolic blood pressure trajectory groups and clinical outcomes

Fan K et al. 2021	24 h SBP groups	Event rate (%) (3 months mRS 3–6)	OR (95%CI)
	Slow drop-low	Not given	5.239 (1.271–21.595)
	Rapid drop-low	Not given	1.969 (0.866–4.477)
	Rapid drop-medium	Not given	Reference
	Rapid drop-high	Not given	2.030 (0.967–4.262)
	Continuous fluctuation-very high	Not given	3.797 (1.486–9.697)
Xu J et al. 2019	7-day SBP groups	Event rate(%) (3 months mRS 3–6)	OR (95%CI)
	Sustained high	25.9	Reference
	Moderate decrease	13.5	0.47 (0.25–0.89)
	Rapid decrease	9.8	0.25 (0.10–0.67)
Changwei Li et al. 2018	7-day SBP groups	Event rate(%) (3 months mRS 3–6)	OR (95%CI)
	High	33.1	Reference
	High-to-moderate-low	28.7	0.81 (0.53–1.25)
	Moderate-high	25.4	0.57 (0.39–0.81)
	Moderate-low	21.1	0.45 (0.31–0.65)
	Low	20.7	0.45 (0.29–0.71)
Jie Xu et al. 2019	7-day SBP groups	Event rate(%) (3 months mRS 3–6)	OR (95%CI)
	Consistent high	23.3	Reference
	Rapid decline from high to low	11.6	0.32 (0.12–0.80)
	Delayed decline from high to low	13.0	0.36 (0.13–1.05)
	Consistent low	12.2	0.37 (0.14–0.97)
	Elevation from low to high	19.3	0.76 (0.31–1.86)
Kim BJ et al. 2018	24h SBP groups	Event rate(%) (1 year composite event*)	HR (95%CI)
	Low	15.1	0.96 (0.83–1.11)
	Moderate	16.4	Reference
	Rapidly stabilized	16.8	1.13 (0.95–1.34)
	Acutely elevated	22.7	1.28 (1.12–1.47)
	Persistently high	22.9	1.67 (1.37–2.04)
Zheng et al. 2021	1 year after discharge SBP groups	Event rate(%) (12–24 months mRS 3–6)	OR (95%CI)
	High-stable	26.39	Reference
	High-decreasing	19.12	0.56 (0.31–0.97)
	Low-increasing	21.17	0.61 (0.33–1.13)
	Low-stable	16.43	0.50 (0.24–0.89)
Petersen NH et al. 2022	3-day SBP groups	Event rate (%) (3 months mRS 3–6)	OR (95%CI)
	Low	47	Reference
	Moderate	58	1.28 (0.95–1.72)
	Moderate-to-high	62	1.49 (1.05–2.08)
	High-to-moderate	71	2.22 (1.52–3.23)
	High	84	3.45 (1.75–6.67)

*a composite of recurrent stroke, myocardial infarction and all-cause death

be summarized that the high SBP trajectory group after AIS is related to poor clinical outcomes, while the rapid decline SBP trajectory group or the moderate-to-low or low SBP trajectory group is associated with relatively better clinical outcomes at different times after stroke.

4 | DISCUSSION

Blood pressure of most acute ischemic stroke patients suddenly rose and spontaneously decreased during the natural history of AIS.[17] The correlation between BP and clinical outcomes in AIS has not been

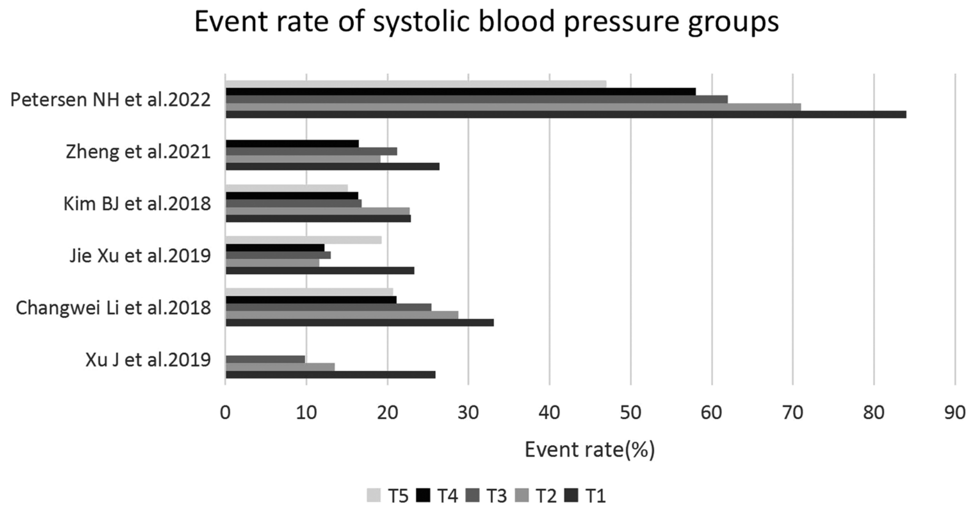

FIGURE 2 Event rate of systolic blood pressure groups in six studies

unified. There are studies have described that hypertension and high BPV are associated with poor prognosis.[18,19] However, among acute ischemic stroke patients with SBP below 100 mmHg at admission and SBP below 120 mmHg at discharge had a significantly increased risk of all-cause mortality, which indicating that hypotensive after AIS may be increasing risk of poor prognosis.[20] A U-shaped association between levels of BP and prognosis has been observed, patients with BP in the middle range have a better prognosis than those with higher or lower extremes.[21]

A growing number of studies are using blood pressure variability to indicate the extent of BP fluctuations in a time period to predict AIS outcomes. Many studies have shown that high BPV after acute ischemic stroke is related to poor prognosis.[18,22,23] From this point of view, blood pressure level and degree of blood pressure fluctuation after AIS have a certain correlation with the prognosis.

The blood pressure change trajectory refers to the longitudinal change of BP in an individual over time. It combines the blood pressure level at a single time point, blood pressure change range and direction, and can more accurately reflect the BP dynamic changes after stroke. Currently, only a few studies have observed the association between systolic blood pressure trajectories and poor outcome of stroke, and the duration and frequency of BP monitoring in these studies are not identical. Due to the heterogeneity of the studies, meta-analysis was not possible and the results of this review must be interpreted with caution. There are undeniably some commonalities observed from this descriptive analysis that persistent high SBP after stroke associated with poor outcomes, while the rapid drop or moderate-to-low or low SBP may reduce the probability of poor prognosis, which is consistent with conclusion of many previous studies.[18,19,21] The reason why changes in BP affect the prognosis of stroke is unclear. In the acute stage of AIS, the brain has dysfunction of self-regulation and becomes highly sensitive to changes in BP. Decreased blood pressure, especially decreased systolic blood pressure, tends to aggravate cerebral ischemia, thus aggravating cerebral edema. When BP increases, blood supply around ischemic penumbra tissue increases, which may lead to post-infarction hemorrhage, aggravate cerebral edema, increase intracranial pressure, and ultimately affect the prognosis.[24,25] The blood pressure trajectory or blood pressure fluctuation pattern over time can more comprehensively reflect the BP information after stroke, some optimal SBP trajectories over time are needed to determine to help guide BP management after stroke.

5 | ADVANTAGE

Most previous studies have attempted to explore the relationship between blood pressure or blood pressure variability and prognosis of AIS. To our knowledge, only a few studies have been devoted to researching the connection between systolic blood pressure trajectory and stroke prognosis. This is the first systematic review to report the prognostic significance of SBP trajectories of AIS patients. This review described the study methods, BP measurement methods, SBP trajectories modeling methods and outcome measurement in detail. From this review, we can infer the rapid decline SBP trajectory group or the moderate-to-low or low SBP trajectory group is associated with relatively better clinical outcomes at different times after stroke, which can provide reference for clinical practice.

6 | LIMITATION

Given the heterogeneity of different studies, the inability to fulfill a meta-analysis was a limitation, limiting the statistical power of the results. While we are also aware of the significance of quantitative analyses, the incapability of meta-analysis is largely because of the lack of similar study designs, blood pressure measurement, systolic blood pressure trajectories and outcome measurement. While these caveats may be addressed by standardized metrics, this will make explanation of meaningful clinical information from studies difficult. This article demonstrated suggests that future research should develop a standardized standard to create a quantitative database that can perform meta-analysis to determine the best SBP group and reliable conclusions about SBP groups' impact on stroke outcomes. We suggest that these criteria may include but not limit to: study population and stroke type; interventions (especially blood pressure management); blood pressure measurement devices, methods, time and interval; SBP trajectory groups; clinical outcome measurement. In addition, we excluded non-English and unpublished literature, which is also a limitation, these studies may be helpful to review the important information of this study.

7 | CONCLUSIONS

This review is limited to the heterogeneity of the included studies, and a meta-analysis cannot be performed to draw reliable conclusions. However, this review qualitatively describes the prognostic significance of the systolic blood pressure trajectories, and these results have reference significance for clinical practice, that is, the rapid decline or moderate-to-low or low SBP group after stroke may have positive prognostic significance. At the same time, this systematic review found significant methodological heterogeneity in SBP trajectory and prognostic indicators. Due to lack of comparisons between BP measurement methods and duration, systolic blood pressure trajectory modeling, the optimal BP measurement method, time, frequency, and SBP trajectory model cannot be accurately obtained. Therefore, more scholars are needed to conduct prospective studies based on standardized criteria to assess the influence of SBP trajectory on prognosis.

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AUTHOR CONTRIBUTIONS

Author 1 (First author) : Search and select literature, data curation, data analysis, Writing original draft and revise, visualization, validation. Author 2: Search and select literature, data curation, data analysis, visualization. Author 3: data curation, data analysis, validation. Author 4: validation, project administration, writing review and revise. Author 5 (Corresponding Author) : conceptualization, methodology, project administration, supervision, writing review and revise.

CONFLICT OF INTEREST

The authors have no competing interests.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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