Blood Pressure Goals in Acute Stroke

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Antihypertensive treatment is highly effective in both primary and secondary prevention of stroke. However, current guideline recommendations on the blood pressure goals in acute stroke are clinically empirical and generally conservative. Antihypertensive treatment is only recommended for severe hypertension. Several recent observational studies showed that the relationship between blood pressure and unfavorable clinical outcomes was probably positive in acute hemorrhagic stroke but J- or U-shaped in acute ischemic stroke with undetermined nadir blood pressure. The results of randomized controlled trials are promising for blood pressure management in hemorrhagic stroke but less so in ischemic stroke. A systolic blood pressure goal of 140 mm Hg is probably appropriate for acute hemorrhagic stroke. The blood pressure goal in acute ischemic stroke, however, is uncertain, and probably depends on the time window of treatment and the use of revascularization therapy. Further research is required to investigate the potential benefit of antihypertensive treatment in acute stroke, especially with regard to the possible reduction of blood pressure variability and more intensive blood pressure lowering in the acute and subacute phases of a stroke, respectively.

Hypertension remains the most powerful risk factor of stroke worldwide and in the stroke prone population in Asia, irrespective of its subtype, either hemorrhagic or ischemic. Antihypertensive drug treatment is highly effective in primary prevention of stroke in patients with hypertension. Current hypertension guidelines recommend initiation of antihypertensive drug treatment in patients with conventionally defined hypertension (systolic/diastolic blood pressure ≥ 140/90 mm Hg) and in high-risk patients with hypertension newly defined in the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines (≥130/80 mm Hg). In most guidelines, blood pressure is recommended to reduce to a level below 140/90 mm Hg and if possible and tolerable to 130/80 mm Hg or even lower. The ACC/AHA guidelines recommend a universal blood pressure goal of 130/80 mm Hg. In fact, the relationship between blood pressure and the risk of stroke is linear and direct, regardless whether blood pressure is measured in the office or out-of-office setting. In addition, the benefit of antihypertensive drug treatment is greater for the prevention of stroke than for other clinical outcomes, such as coronary events. Indeed, the relative risk reduction for approximately each 10/5 mm Hg reduction in systolic/diastolic blood pressure was about 42% for stroke and 14% for coronary events in patients with systolic and diastolic hypertension. The corresponding risk reductions in patients with isolated systolic hypertension were 30% and 23%, respectively. No J-curve has ever been observed for stroke, as for other clinical outcomes such as coronary events.

In patients with a history of cerebrovascular disease, antihypertensive drug treatment is still highly effective in the prevention of recurrent stroke. In the China
Post-stroke Antihypertensive Treatment (PATS) trial in patients with a stabilized stroke, antihypertensive drug treatment with a thiazide-like diuretic indapamide 2.5 mg per day reduced systolic/diastolic blood pressure by 5/2 mm Hg and the incidence of recurrent stroke by 29%.15,16 The multinational Perindopril Protection Against Stroke Recurrence Study (PROGRESS) confirmed the beneficial effects of antihypertensive drug treatment in the prevention of recurrent stroke in patients with a stabilized recent cerebrovascular disease.18 Antihypertensive drug treatment with either perindopril alone (4 mg per day) or perindopril and indapamide combination reduced systolic/diastolic blood pressure by 9/4 mm Hg and the incidence of recurrent stroke by 28%.18 When these 2 trials were combined with four other antihypertensive treatment trials in patients with a history of cerebrovascular disease, the overall reduction in the risk of recurrent stroke was 25%,15 with approximately a mean reduction of 7/3 mm Hg in systolic/diastolic blood pressure.19

Several subsequent trials included both patients with a stabilized recent stroke and those with an acute stroke, and showed modest or no benefit of blood pressure lowering.20,21 In the Prevention Regimen for Effectively Avoiding Secondary Strokes (PROFESS) trial in 20,332 patients with a recent ischemic stroke (median interval from stroke to randomization 15 days), telmisartan 80 mg per day reduced systolic/diastolic blood pressure by 3.8/2.0 mm Hg during a mean follow-up of 2.5 years.20 The risk reduction in recurrent stroke was only 5% and statistically nonsignificant (P = 0.2).20 In the Secondary Prevention of Small Subcortical Strokes (SPS3) trial in 3020 patients with a recent lacunar stroke (median time from qualifying stroke to randomization 62 days), systolic blood pressure lowering with a lower target (<130 mm Hg), compared with higher-target (130–149 mm Hg), reduced systolic blood pressure from 138 mm Hg to 127 mm Hg by 11 mm Hg during a mean follow-up of 3.7 years.21 The risk reduction in the lower than higher target group was non-significant for all recurrent stroke (hazard ratio 0.81, P = 0.08), but significant for intracerebral hemorrhage (hazard ratio 0.37, P = 0.03).21

In the acute phase of a stroke, blood pressure management is apparently much more complex than for primary prevention of stroke in patients with hypertension or for secondary prevention in patients with a stabilized stroke. A key question is at what level of blood pressure do we need to initiate antihypertensive treatment and how low may we reduce blood pressure. A similarly important but even more difficult question is at what time after a stroke do we need to initiate antihypertensive treatment. In the past 2 decades, a number of observational studies and randomized clinical trials addressed these questions in patients with various subtypes of stroke. In the present review article, we first summarize the current guideline recommendations in this particular regard, and then the recent observational and clinical trial evidence on the blood pressure goals in acute stroke.

SEARCH STRATEGY AND SELECTION OF PUBLICATIONS

A total of 12,464 abstracts and full-text articles were systematically retrieved from electronic databases (PubMed and Embase) and manual search on January 28, 2022. For the search from electronic databases, we used terms: “blood pressure”, “acute”, “stroke”, “intracerebral hemorrhage”, “brain hemorrhage”, and “cerebral hemorrhage”. We also searched manually from the reference lists of identified articles.

Eligible studies were published in full-text articles in English, which presented data from prospective or retrospective observational studies or randomized clinical trials. To be eligible for inclusion, an observational study should have investigated the relationship between blood pressure measured within 14 days of an acute stroke and clinical outcomes, and a randomized clinical trial should have compared various goals of blood pressure control or various intensities of antihypertensive treatment. We also searched and reviewed current guidelines for the blood pressure management in acute stroke. Finally, we presented in this review 5 guidelines,22–26 33 observational studies,27–59 and 12 randomized clinical trials (Figure 1).60–71

CURRENT GUIDELINE RECOMMENDATIONS

In addition to the European Stroke Organization guidelines on blood pressure management in acute ischemic and hemorrhagic stroke,22 several recent stroke-specific guidelines also provide detailed recommendations on blood pressure management in the acute phase of hemorrhagic23,24 and ischemic stroke (Table 1).25,26 The recommendations for hemorrhagic stroke are straightforward and consistent between various guidelines.22–24 The recommendations for ischemic stroke, however, are complicated, not only because of weak evidence, but also because of the complexity in the treatment, such as the use of intravenous thrombolysis and more recently arterial mechanical thrombectomy.22,25,26

The recent guideline recommendations for blood pressure management in acute hemorrhagic stroke were heavily influenced by the results of the intensive blood pressure reduction in an acute intracerebral hemorrhage trial (INETERACT), which is the largest ever blood pressure lowering trial in acute intracerebral hemorrhage.61 Although the benefit of intensive blood pressure lowering to a level of 140 mm Hg systolic was only borderline significant, it provided evidence that early intensive blood pressure was safe and probably beneficial in functional recovery in those patients with acute hemorrhagic stroke and systolic blood pressure of 150–220 mm Hg.61 The AHA/American Stroke Association (ASA) guidelines substantially simplified the recommendations that in patients with a systolic blood pressure of 150–220 mm Hg and without contraindication to acute blood pressure treatment acute systolic blood pressure lowering to 140 mm Hg is safe and can be effective for improving functional outcome.22 This AHA/ASA guidelines continued to recommend aggressive blood pressure reduction with a continuous intravenous infusion and frequent blood pressure monitoring in those patients with a systolic blood pressure of ≥220 mm Hg. The subsequent Canadian24 and European25 guidelines provided similar recommendations.

The complexity of blood pressure management in acute ischemic stroke is mainly related to the use of
intravenous thrombolytic therapy and arterial mechanical thrombectomy. In general, the current guidelines are conservative in recommending blood pressure lowering treatment in acute ischemic stroke unless systolic/diastolic blood pressure is extremely high, e.g., >220/120 mm Hg. However, the current guidelines recommend that systolic/diastolic blood pressure should be reduced to and maintained at a level below 185/110 mm Hg and 180/105 mm Hg in those patients who undergo treatment with intravenous thrombolytic therapy and arterial mechanical thrombectomy, respectively.

The recommendations of these hypertension guidelines are generally conservative in blood pressure management in acute intracerebral hemorrhage as well as acute ischemic stroke. For instance, these guidelines do not recommend immediate blood pressure lowering in patients with a hemorrhagic stroke and a systolic blood pressure of 150–220 mm Hg, because of safety concerns on renal outcomes in the Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH)-2 trial. However, these guidelines do recommend timely start or restart of antihypertensive drug treatment for secondary prevention. The European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines recommend that for stable patients who remain hypertensive (≥140/90 mm Hg) more than 3 days after an acute ischemic stroke, initiation, or reintroduction of blood pressure-lowering medication should be considered.

**OBSERVATIONAL EVIDENCE**

A number of observational studies investigated the association between blood pressure at various timepoints after a stroke and short- and long-term clinical outcomes. These studies focused on the level of blood pressure at admission or in the initial hours or days of hospitalization. Most of these studies investigated systolic and diastolic components of blood pressure. Some studies also included mean arterial pressure and pulse pressure. However, there was no standardized protocol for blood pressure measurement in the early critical phase of a stroke.
### Table 1. Current guideline recommendations on blood pressure goals in acute stroke

| Guideline                  | Clinical situation                                                                 | Blood pressure lowering and monitoring                                                                 |
|----------------------------|------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| **Hemorrhagic stroke**     |                                                                                    |                                                                                                          |
| AHA/ASA 2015               | SBP 150–220 mm Hg and without contraindication to acute BP treatment               | Acute lowering of SBP to 140 mmHg is safe and can be effective for improving functional outcome.         |
|                            | SBP > 220 mm Hg                                                                     | It may be reasonable to consider aggressive reduction of BP with a continuous intravenous infusion and frequent BP monitoring. |
| Canadian 2020              |                                                                                    | A SBP threshold at an individual target of < 140–160 mm Hg for the first 24–48 hours post stroke onset may be reasonable. |
| ESO 2021                   | Hyperacute (<6 hours) intracerebral hemorrhage                                      | SBP < 140 mm Hg (and > 110 mm Hg) to reduce hematoma expansion                                        |
|                            | Eligible for thrombolytic therapy and SBP/DBP > 185/110 mm Hg                     | SBP/DBP < 185/110 mm Hg before intravenous fibrinolytic therapy                                        |
|                            | Patients for whom intra-arterial therapy is planned and who have not received intravenous thrombolytic therapy | It is reasonable to maintain SBP/DBP ≤ 185/110 mm Hg before the procedure.                            |
|                            | SBP/DBP > 220/120 mm Hg                                                             | Reduce BP by ~15%, and not > 25%, over the first 24 hours with further gradual reduction thereafter to targets for long-term secondary stroke prevention |
|                            | Eligible for thrombolytic therapy and SBP/DBP > 185/110 mm Hg                     | SBP/DBP < 185/110 mm Hg before bolus and below 180/105 mm Hg after bolus, and for 24 hours after alteplase infusion |
|                            | Patients who have elevated BP and are otherwise eligible for treatment with intravenous alteplase | SBP/DBP < 185/110 mm Hg before intravenous fibrinolytic therapy                                        |
|                            |                                                                                     | It is reasonable to maintain SBP/DBP ≤ 185/110 mm Hg before the procedure.                            |
|                            | SBP/DBP > 220/120 mm Hg                                                             | Reduce BP by ~15%, and not > 25%, over the first 24 hours with further gradual reduction thereafter to targets for long-term secondary stroke prevention |
| ESO 2021                   | SBP/DBP < 220/110 mm Hg and not treated with intravenous thrombolysis or mechanical thrombectomy | No routine use of BP lowering agents at least in first 24 hours following symptom onset, unless necessary for a specific comorbid condition |
|                            | Undergoing treatment with intravenous thrombolysis (with or without mechanical thrombectomy) | SBP/DBP < 185/110 mm Hg before bolus and below 180/105 mm Hg after bolus, and for 24 hours after alteplase infusion |
|                            | Large vessel occlusion undergoing mechanical thrombectomy (with or without intravenous thrombolysis) | SBP/DBP < 180/105 mm Hg during and 24 hours after mechanical thrombectomy                              |

Guidelines are listed in the ascending order of the year of publication for hemorrhagic and ischemic stroke separately.

Abbreviations: AHA/ASA, American Heart Association/American Stroke Association; BP, blood pressure; DBP, diastolic blood pressure; ESO, European Stroke Organization; SBP, systolic blood pressure.
Table 2. Observational studies on the relationship between blood pressure and clinical outcomes in acute hemorrhagic and ischemic stroke since 2002

| First author and year of publication | Design | Time windowa | No. of Patients | Men (%) | Age, years | Baseline SBP/DBP, mm Hg | Anti-HT (%) | Primary outcome | Major findings on blood pressure goals |
|-------------------------------------|--------|--------------|----------------|---------|------------|-------------------------|-------------|----------------|-------------------------------------|
| **Hemorrhagic stroke**              |        |              |                |         |            |                         |             |                |                                     |
| Koga, 201227                        | PP     | 3 h          | 211            | 62      | 66         | 202/108                 | NA          | Neurological deterioration within 72 h (GCS decrement ≥ 2 points or NIHSS increment ≥ 4 points) and SAE to stop IV nicardipine within 24 h | Treating to SBP ≤ 160 mm Hg was safe and feasible. |
| Sakamoto, 201328                    | PP     | 3 h          | 211            | 62      | 65         | 200/80                  | NA          | Neurological deterioration within 72 h (GCS decrement ≥ 2 or NIHSS increment ≥ 4), hematoma expansion > 33% from baseline to 24 h, and mRS 4–6 at 3 months | A mean achieved SBP ~130 mm Hg was associated with the lowest odds ratios for worse outcomes. |
| Rodriguez-Luna, 201429             | RT     | 6h           | 117            | 58      | 71         | 172/92                  | NA          | Hematoma growth at 24 h, early neurological deterioration, 24 h and 90-day mortality, and poor outcome | SBP lowering to ≤ 160 mm Hg minimized the deleterious effect on 24 h outcomes. |
| Mustanoja, 201830                  | RT     | 24h          | 334            | 61      | 40         | 155/92                  | 51          | 3-month and long-term (median of 12 years) mortality | SBP ≥ 160 mm Hg had higher 3-month and long-term mortality. |
| Zhao, 201931                       | RT     | 6 h          | 659            | 71      | 65         | 165/101                 | NA          | Mortality, rates of operation, length of ICU stay, and mRS at 90 days | SBP < 140/90 mm Hg had smaller hematoma growth and lower rates of operation and mRS. |
| Francoeur, 202132                  | RT     | 24 h         | 384            | 61      | 66         | 179/96                  | NA          | Death or moderate-to-severe disability at 3 months (mRS 4–6) | SBP > 140 mm Hg had poor outcome. |
| **Ischemic stroke without thrombolysis or mechanical thrombectomy** |        |              |                |         |            |                         |             |                |                                     |
| Castillo, 200433                   | PP     | 24 h         | 304            | 52      | 72         | 179/97                  | 22.1        | Early neurological deterioration at 48 h and neurological deficit and mortality at 90 days | U-shaped association with a nadir SBP/DBP at admission and 24 h 180/100 mm Hg; SBP/DBP ↓ ≥20 mm Hg within the first 24 h had poor prognosis. |
| Vemmos, 200434                     | PP     | 24 h         | 1121           | 57      | 71         | NA                     | NA          | Mortality at 1 and 12 months | Patients with admission SBP > 220 mm Hg or < 120 mm Hg had higher mortality. |
| Abboud, 200635                     | PP     | 24 h         | 230            | 64      | 67         | 150/84                  | NA          | Mortality or dependency (mRS > 3) at 10 days and 6 months | SBP ≥ 165 mm Hg had poor outcome at 10 days and 6 months. |
| Sartori, 200636                    | PP     | 24 h         | 71             | 77      | 76         | 160/86                  | 22.4        | Mortality at 3 months | MAP decrease > 5 mm Hg had better outcome. |
| Armario, 200837                    | PP     | 3 h          | 100            | 51      | 74         | 163/88                  | 2.0         | Functional recovery (mRS ≤ 2) at discharge and 3 months | SBP ≥ 185 mm Hg had poor outcome at discharge and 3 months. |
| Weiss, 201338                      | PP     | 24 h         | 177            | 50      | 84         | 151/78                  | 51          | Functional status (mRS) and mortality (≤5 years) | 24 h mean SBP > 160 mm Hg was associated with higher mortality. |
| Hao, 201439                        | PP     | 2–270 hb     | 215            | 60      | 60         | 142/84                  | 40.5        | Death or disability (mRS > 2) at 3 months | SBP/DBP 120–159/70–89 mm Hg had the lowest risk. |
| First author and year of publication | Design | Time window | No. of Patients | Men (%) | Age, years | Baseline SBP/DBP, mm Hg | Anti-HT (%) | Primary outcome | Major findings on blood pressure goals |
|--------------------------------------|--------|-------------|----------------|---------|------------|------------------------|------------|----------------|-------------------------------------|
| Ishitsuka, 201440                    | PP     | 24 h        | 1874           | 62      | 70         | 149/81                 | 33.4       | Neurological recovery (NIHSS decrement ≥ 4 in hospital or = 0 at discharge); early neurological deterioration (NIHSS increment ≥ 2 in hospital); death or disability (mRS > 2) at 3 months | SBP/DBP ≥ 144/89 mm Hg predicted poor outcome. |
| Wohlfahrt, 201541                    | PP     | 24 h        | 532            | 59      | 66         | NA                    | 62         | Mortality during a median follow-up of 66 weeks | All-cause mortality increased with admission MBP < 100 mm Hg and discharge SBP < 120 mm Hg. |
| Mustanoja, 201642                    | PP     | 24 h        | 1004           | 63      | 44         | 141/86                 | 36         | Recurrent stroke during a median follow-up of 8.9 years | SBP/DBP ≥ 160/100 mm Hg had a higher risk of recurrent stroke. |
| Bangalore, 201743                    | PP     | 4.5 h       | 309,611        | 48      | 74         | NA                    | NA         | In-hospital mortality, not discharged, inability to ambulate at discharge and hemorrhagic complications due to thrombolysis | U-shaped or J-shaped association with a nadir at 150/70 mm Hg |
| Kang, 201944                         | RT     | 48 h        | 3723           | 59      | 67         | 134/-                  | NA         | Unfavorable outcome (mRS > 2) at discharge and time to composite cardiovascular event of stroke, myocardial infarction, and vascular death for 1-year follow-up. | SBP > 156 mm Hg had worse outcome than SBP ≤ 133.2 mm Hg. |
| Ajinkya, 202045                      | RT     | 24 h        | 1232           | 49      | 67         | 158/85                 | NA         | Mortality and mRS ≤ 2 at 90 days | SBP ≤ 139–157 mm Hg in the tPA group and ≤ 137–181 mm Hg in the non-tPA group had a lower risk of 90-day mortality. |

**Ischemic stroke with thrombolysis and mechanical thrombectomy**

**Intravenous thrombolysis**

| Wu, 201746                           | RT     | Pre & post  | 383             | 73      | 61         | 148/-                  | 44.6       | Unfavorable outcome (mRS 3–6) at 3 months | Post thrombolysis SBP ≤ 160 mm Hg had a favorable outcome. |
| He, 202147                           | RT     | Pre, post, 24 h, & 7 d | 510 | 65 | 65 | 158/90 | 42.6 | mRS ↓ ≥ 2 points or 0–3 at 3 months | SBP < 148 mm Hg in the first 24 h after thrombolysis then SBP 127–138 mm Hg would be beneficial. |

**Mechanical thrombectomy**

| Goyal, 201748                         | PP     | 24 h post   | 217             | 50      | 62         | 158/90                 | 19.8       | Functional recovery (mRS 0–2) at 3 months | SBP/DBP < 160/90 mm Hg during the first 24 h after MT was associated with a lower risk of 3-month mortality. |
| Maier, 201749                         | PP     | 12 h        | 1042            | 54      | 68         | 149/81                 | NA         | All-cause mortality, good outcome (mRS of 0–2) at 3 months, and ICH | Baseline SBP ≥ 177 mm Hg predicted unfavorable outcome. |
| Anadani, 201950                      | PP     | 24 h post   | 298             | 49      | 67         | 146/-                  | 61.4       | Mortality and unfavorable outcome (mRS > 2) at 3 months | SBP < 120 mm Hg at 24 h after MT had a better 90-day outcome and lower mortality. |
| First author and year of publication | Design | Time window | No. of Patients | Men (%) | Age, years | Baseline SBP/DBP, mm Hg | Anti-HT (%) | Primary outcome | Major findings on blood pressure goals |
|-------------------------------------|--------|-------------|----------------|---------|------------|-------------------------|-------------|----------------|--------------------------------------|
| Anadani, 2019<sup>51</sup>          | RT     | 24 h post   | 1245           | 51      | 69         | 144/80                  | NA          | 90-day mRS, symptomatic ICH, mortality, and hemicraniectomy | High blood pressure with higher risk. |
| van den Berg, 2020<sup>52</sup>     | PP     | 6.5 h       | 3180           | 48      | 72         | 150/82                  | 54          | Mortality and unfavorable outcome (mRS > 2) at 3 months | J-shaped association with a nadir at 150/81 mm Hg of admission SBP/DBP |
| An, 2021<sup>53</sup>               | RT     | 24 h post   | 164            | 68      | 65         | 146/80                  | NA          | ICH during the first 24 h after MT | Optimal maximum SBP/DBP ≤ 155/92.5 mm Hg |
| Chen, 2021<sup>54</sup>             | PP     | Admission, pre, & post | 139     | 41      | 76         | 169/93                  | NA          | Favorable outcome (mRS 0–3) at 3 months | Admission SBP ≤ 187 mm Hg and MAP ≤ 125 mm Hg; Pre-MT SBP ≤ 163 mm Hg; and MAP ≤ 117 mm Hg |
| Gigliotti, 2021<sup>55</sup>        | RT     | 24 h post   | 117            | 47      | 65         | NA                      | 27.3        | mRS at discharge and 3 months, incidence of ICH, malignant cerebral edema, mortality at 3 months, and discharge disposition | SBP ≥ 180 mm Hg predicted poor functional outcome at discharge. SBP ≥ 160 mm Hg resulted in an increased odds of malignant cerebral edema. |

**Intravenous thrombolysis or mechanical thrombectomy**

| Choi, 2019<sup>56</sup>            | PP     | 72 h        | 1540           | 56      | 69         | 130/82                  | NA          | mRS 0–2 at 3 months | SBP/DBP ≤ 130/80 mm Hg was associated with favorable outcome. |

**Mixed (hemorrhagic/ischemic) stroke**

| Okumura, 2005<sup>57</sup>          | PP     | 24 h        | 1097/1004/     | 53/56   | 64/70      | 182/99                  | NA          | Mortality at 30 days | For ICH, SBP/DBP ≥ 230/120 mm Hg higher mortality; For AIS, U-shaped association with a nadir at 150–169/110–110 mm Hg. |
| Zhang, 2008<sup>58</sup>            | RT     | 24 h        | 1760/2178      | 60/62   | 56/61      | 172/104                 | 152/92      | Death and disability/dependence during hospitalization | For ICH, ≥140 mm Hg, higher risk; For AIS, no association. |
| Furlan, 2018<sup>59</sup>           | RT     | 48 h        | 45/101         | 53/55   | 64/68      | 173/79                  | 156/91      | All-cause mortality during the first 7 days | For ICH, no association; For AIS, SBP ≤ 131 mm Hg, higher mortality. |

Studies are listed in the order of the year of publication with each subsection.

Abbreviations: AIS, acute ischemic stroke; Anti-HT, anti-hypertensive agents; BP, blood pressure; DBP, diastolic blood pressure; END, Early Neurological Deterioration; ICH, intracerebral hemorrhage; ICU, intensive care unit; IV, intravenous; MAP, mean arterial pressure; mRS, modified Rankin Scale; MT, mechanical thrombectomy; mTICI, modified Treatment in Cerebral Ischemia; NA, not available; NIHSS, National Institutes of Health Stroke Scale; PP, prospective; RT, retrospective; SBP, systolic blood pressure; tPA, tissue plasminogen activator.

<sup>a</sup>Time windows refers to time from the onset of stroke to admission.

<sup>b</sup>Patients with severe intracranial stenosis or occlusion.
**Hemorrhagic Stroke**

Our literature search identified one prospective observational study with 2 publications and 4 retrospective analysis reports. The only prospective study required that patients had an entry systolic blood pressure of at least 180 mm Hg. The mean baseline systolic and diastolic blood pressure in this prospective study was 202/108 mm Hg and much higher than that in the retrospective studies without any entry criteria of blood pressure (from 155/92 mm Hg to 179/96 mm Hg). The prospective study showed that treating systolic blood pressure to a level below 160 mm Hg was safe and feasible. In a post-hoc analysis of this prospective study, the investigators further analyzed the relationship between achieved systolic blood pressure and clinical outcomes, and found that an approximately 130 mm Hg of the achieved systolic blood pressure was associated with the lowest odds ratio for worse clinical outcomes. The retrospective analyses consistently showed that a lower systolic blood pressure below 160 mm Hg was associated with better clinical outcomes.

**Ischemic Stroke**

The number of observational studies for acute ischemic stroke was much greater than for acute hemorrhagic stroke. These studies were mostly prospectively designed and dealt with 2 different situations of treatment, i.e., without or with intravenous thrombolysis and arterial mechanical thrombectomy.

In the absence of the interventional revascularization therapy, J- or U-shaped relationship between blood pressure and clinical outcomes after an acute ischemic stroke was observed in almost all studies including the US Get With The Guidelines-Stroke registry with a huge number of patients (n = 309,611). Both high and low blood pressures at admission and the initial hours after an acute ischemic stroke were associated with unfavorable clinical outcomes. However, the nadir was different between these studies from 120 to 185 mm Hg of systolic blood pressure, but mostly around 150–160 mm Hg. The difference might have been influenced by several factors. Among others, the timepoint of blood pressure measurement might be crucial. The nadir was higher in the analysis on admission blood pressure than mean blood pressure during the first 24– or 48-hours after stroke onset. There was often a spontaneous blood pressure decline after admission even without any blood pressure lowering medication.

With the shortening of the time from door to needle and the technological advancing, there is an increasing proportion of patients who receive either intravenous thrombolysis or arterial mechanical thrombectomy. Under the circumstances of these interventions, the relationship between blood pressure and clinical outcomes after an acute ischemic stroke is becoming even more complicated. Blood pressure can be measured at admission and pre- or post-procedure. Two retrospective studies consistently showed that patients with a lower post-thrombolysis systolic blood pressure had favorable clinical outcomes with a nadir at 160 and 148 mm Hg, respectively.

The prognostic significance of blood pressure in patients receiving arterial mechanical thrombectomy was investigated in several prospective and retrospective studies. These studies were consistent in showing that lower blood pressure was associated with better clinical outcomes. However, the timepoint of blood pressure measurement again was an issue, including admission, pre-procedure, and hours and days post-procedure. How low a blood pressure was associated with a favorable outcome is also an issue. When admission blood pressure was considered, the threshold was approximately 160–180 mm Hg. When post-thrombectomy blood pressure was considered, it was about 20 mm Hg lower, down to 120 mm Hg. The procedure probably increases the likelihood of benefit from blood pressure lowering in patients with an acute ischemic stroke. Indeed, a blood pressure below 130 mm Hg systolic and 80 mm Hg diastolic was associated with favorable clinical outcomes in a study in patients treated with intravenous thrombolysis or mechanical thrombectomy and with blood pressure data collected within 72 hours of an acute ischemic stroke.

**Mixed Hemorrhagic and Ischemic Stroke**

Three studies included both patients with acute intracerebral hemorrhage and those with acute ischemic stroke. These studies allowed comparison between these 2 subtypes of stroke with regard to the relationship between blood pressure and clinical outcomes. Higher blood pressure was associated with a higher risk of unfavorable clinical outcomes in patients with hemorrhagic stroke in 2 of the 3 studies. A J-shaped association was observed in patients with acute ischemic stroke in 2 of the 3 studies. Again, the nadir was different between these studies for both hemorrhagic and ischemic stroke, similarly as the abovementioned studies.

**CLINICAL TRIAL EVIDENCE**

Observational studies provided useful evidence for blood pressure management in acute stroke. However, the findings are generally hypothesis-generating and need to be confirmed in randomized controlled trials. In the past 2 decades, several trials have been conducted to test whether blood pressure lowering is beneficial in the prevention of mortality and dependency in acute hemorrhagic or ischemic stroke or both (Table 3). Most of these randomized antihypertensive treatment trials in acute stroke were with a clearly defined goal of blood pressure lowering. Usually, any antihypertensive treatment could be used to achieve the goal of blood pressure control. Two studies, however, were without a goal of blood pressure lowering but with a standardized antihypertensive treatment regimen. Although a trial with the latter design does not have a priori hypothesis of blood pressure targets, the achieved blood pressure during treatment also provides guidance on blood pressure goals.
| First author and year of publication | Time window* | No. of patients | Men (%) | Mean age at baseline, years | Mean SBP/DBP at baseline, mm Hg | Intervention vs. control | Primary outcome | Major findings on blood pressure goals |
|--------------------------------------|--------------|----------------|---------|-----------------------------|----------------------------------|-------------------------|----------------|---------------------------------------|
| **Hemorrhagic stroke**                |              |                |         |                             |                                  |                         |                |                                       |
| Anderson (INTERACT-1), 2008          | 6 h          | 203/201        | 61.69   | 63/62                       | 180/101 vs. 182/105              | Intensive (<140 mm Hg) vs. standard (<180 mm Hg) | Proportional change in hematoma volume at 24 h | Intensive treatment was feasible and tolerated, and reduced hematoma growth. |
| Anderson (INTERACT-2), 2013          | 6 h          | 1399/1430      | 64.2/61.7 | 63/64                       | 179/101 vs. 179/101              | Intensive (<140 mm Hg within 1 h) vs. standard (<180 mm Hg) | Death or major disability (mRS 3–6) at 90 days | Intensive treatment did not result in a significant reduction in death and severe disability. |
| Qureshi (ATACH-2), 2016              | 4.5 h        | 500/500        | 60.8/63.2 | 62.0/61.9                   | 200/- vs. 201/-                 | Intensive (SBP 110–139 mm Hg) vs. standard (SBP 140–179 mm Hg) | Mortality or dependency (mRS 4–6) at 3 months | Intensive treatment did not result in a lower rate of outcome than standard treatment. |
| Gupta, 2018                          | 72 h         | 59/59          | 66/77   | 65.1/62.8                   | 175.1/109.8 vs. 178.5/111.7     | Tight MAP control (<115 mm Hg) vs. conventional control (<130 mm Hg) | mRS at 90 days | MAP can be lowered to ≤ 115 mm Hg without increasing the odds of a poor clinical outcome at 90 days. |
| **Ischemic stroke**                  |              |                |         |                             |                                  |                         |                |                                       |
| He (CATIS), 2014                     | 48 h         | 2038/2033      | 64.6/63.3 | 62.1/61.8                   | 166.7/96.8 vs. 165.6/96.5       | Lowering SBP 10–25% within the first 24 h and SBP/DBP < 140/90 mm Hg within 7 days vs. discontinue antihypertensive drugs | Mortality or dependency (mRS > 3) at 2 weeks or discharge | Primary outcome did not differ between treatment groups (mean SBP at day 7 was 137.3 and 146.5 mm Hg in the active and control groups, respectively). |
| Anderson (ENCHANTED), 2019           | 6 h          | 1081/1115      | 62.9/61.1 | 66.7/67.1                   | 165.4/91.2 vs. 165.2/90.7       | Intensive (SBP 130–140 mm Hg within 1 h) vs. standard (SBP < 180 mm Hg) | Functional status (mRS) at 3 months | Intensive treatment did not result in a lower rate of outcome than standard treatment. |
| Nasi (MAPAS), 2019                   | 12 h         | 77/75/66       | 56/57/47 | 68/69/67                    | 153/- vs. 163/- vs. 178/-       | Maintain SBP during 24 h within: 140–160 mm Hg vs. 161–180 mm Hg vs. 181–200 mm Hg | Favorable outcome (mRS 0–2) at 3 months | Targeting SBP 160–180 mm Hg tended to have favorable outcome; ICH occurred more frequently in Group 3 (181–200 mm Hg). |
| Mazighi (BP-TARGET), 2021            | Post MT      | 158/160        | 51/45   | 77/76                       | 155/86 vs. 152/85               | Intensive (SBP 100–129 mm Hg) vs. standard (SBP 130–185 mm Hg) | The rate of radiographic intraparenchymal hemorrhage at 24–36 h | Intensive SBP target after successful endovascular therapy did not reduce the rate of radiographic intraparenchymal hemorrhage at 24–36 h as compared with the standard SBP target. |
Table 3. Continued

| First author and year of publication | Time windowa | No. of patients | Men (%) | Mean age at baseline, years | Mean SBP/DBP at baseline, mm Hg | Intervention vs. control | Primary outcome | Major findings on blood pressure goals |
|-------------------------------------|--------------|----------------|---------|-----------------------------|--------------------------------|-------------------------|----------------|--------------------------------------|
| **Mixed hemorrhagic and ischemic stroke** |
| Potter (CHHIPS), 200968 | 36 h | 113/59 | 57/53 | 74/74 | 182/95 vs. 181/96 | Active treatment (labetalol or lisinopril, targeting SBP 145–155 mm Hg or a reduction 15 mm Hg) vs. placebo | Mortality or dependency (mRS > 3) at 2 weeks | Active treatment did not influence the primary outcome, but reduced mortality at 3 months. |
| Robinson (COSSACS), 201069 | 48 h | 379/384 | 55/56 | 74/74 | 149/80 vs. 150/81 | Continue vs. stop pre-existing antihypertensive drug treatment | Mortality or dependency (mRS > 3) at 2 weeks | Continued treatment lowered SBP/DBP (140/76 mm Hg) and did not increase adverse events, compared to stopped treatment (153/84 mm Hg). |
| Sandset (SCAST), 201170 | 30 h | 1017/1012 | 60/56 | 71/71 | 171.2/90.3 vs. 171.6/90.6 | Candesartan vs. placebo | Composite endpoint (vascular death, MI, or stroke) and mRS at 6-months | Active treatment (147/82 mm Hg) had a higher risk of poor functional outcome than control group (152/84 mm Hg), but similar risk for composite vascular endpoint. |
| Yuan (CHASE), 202171 | 72 h | 242/241 | 55.8/55.6 | 66.4/66.0 | 174.3/96.6 vs. 173.1/97.2 | Individualized treatment (with 10–15% ↓ in SBP 130–180 mm Hg within 2 h and maintain for 1 week) vs. standard (SBP < 200 mm Hg in AIS and < 180 mm Hg in ICH within 1 week) | Dependency (mRS > 3) at 3 months | Individualized treatment did not result in a lower rate of outcome than standard treatment. |

Studies are listed in the order of the year of publication with each subsection. For explanations on the acronyms of trials, see the text.

Abbreviations: AIS, acute ischemic stroke; DBP, diastolic blood pressure; ICH, intracerebral hemorrhage; MI, myocardial infarction; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

aTime windows refers to time from the onset of stroke to admission.
**Hemorrhagic Stroke**

Four randomized controlled trials investigated blood pressure targets in acute hemorrhagic stroke.\(^60-63\) In 3 trials, patients with an acute intracerebral hemorrhage within 4.5 to 6 hours were enrolled, and the goal of intensive blood pressure lowering was a systolic blood pressure below 140 mm Hg.\(^60-62\) In another trial, patients with less acute hemorrhagic stroke within 72 hours were enrolled, and the goal of intensive blood pressure lowering was a mean arterial pressure below 115 mm Hg.\(^63\)

The INTERACT-1 trial tested the feasibility of early lowering of elevated blood pressure in 404 patients with an acute intracerebral hemorrhage within 6 hours of onset and elevated systolic blood pressure (150–220 mm Hg).\(^60\) Intensive blood pressure lowering treatment (target systolic blood pressure 140 mm Hg) reduced systolic blood pressure to 153 mm Hg at 1 hour from randomization and 146 mm Hg from 1 to 24 hours after randomization. The corresponding differences were 13.3 mm Hg and 10.8 mm Hg, respectively, from that of the standard guideline-based blood pressure management group (target systolic blood pressure 180 mm Hg). Proportional change in hematoma volume at 24 hours after randomization, which was the primary endpoint, tended to be smaller in the intensive than standard blood pressure lowering group (13.7\% vs. 36.3\%, \(P = 0.04\)).

![Figure 2](image-url)
Intensive blood pressure lowering treatment did not alter the risks of adverse events or secondary clinical outcomes at 90 days. The trial showed that early intensive blood pressure lowering treatment was clinically feasible and well tolerated, and built the basis for an outcome trial.

The INTERACT-2 trial had a similar design as the INTERACT-1 trial, but was an outcome study. The primary endpoint was death or major disability (a score of 3 to 6 on the modified Rankin scale, in which a score of 0 indicates no symptoms, a score of 5 indicates severe disability, and a score of 6 indicates death) at 90 days. In 2,794 patients with a spontaneous intracerebral hemorrhage within 6 hours of onset and elevated systolic blood pressure (150–220 mm Hg), intensive blood pressure lowering (targeting systolic blood pressure 140 mm Hg) did not result in a significant reduction in the rate of mortality and disability (odds ratio 0.87, \( P = 0.06 \)). An ordinal analysis, however, showed significantly lower modified Rankin scores with intensive treatment (odds ratio for greater disability 0.87, \( P = 0.04 \)), indicating improved functional outcomes with intensive blood pressure lowering. The results of several post-hoc analyses of INTERACT-2 suggested that lower blood pressure variability (Figure 2) and lower achieved blood pressure level (Figure 3) were associated with favorable clinical outcomes and raised hypotheses for future research.

The ATACH-2 trial was in design similar to the INTERACT-2 trial, but administered a standardized blood pressure lowering regimen with intravenous nicardipine to lower blood pressure to a systolic blood-pressure target of 110 to 139 mm Hg (intensive treatment) or a target of 140 to 179 mm Hg (standard treatment) in patients with an acute intracerebral hemorrhage within 4.5 hours after symptom onset. Enrollment was stopped because of futility after a prespecified interim analysis in 1,000 randomized patients. The mean minimum systolic blood pressure during the first 2 hours was 128.9 mm Hg and 141.1 mm Hg in the intensive and standard-treatment groups, respectively. The primary outcome (death or disability, defined by modified Rankin scale score of 4 to 6, at 3 months after randomization) was not different between the 2 treatment groups (intensive vs. standard, relative risk 1.04, 95% confidence interval 0.85–1.27). However, the rate of renal adverse events within 7 days after randomization was significantly higher in the intensive-treatment than standard-treatment group (9.0% vs. 4.0%, \( P = 0.002 \)).

Around similar period of time, a multicentric trial was conducted in India in 118 randomized patients with spontaneous intracerebral hemorrhage within 72 hours of onset to compare tight (target mean arterial pressure 115 mm Hg) with conventional blood pressure control (target mean arterial pressure 130 mm Hg). Mean arterial pressure was 110 mm Hg and 120 mm Hg in the intensive and conventional blood pressure control groups, respectively. The primary outcome was not different between the 2 blood pressure control groups (median modified Rankin Scale at 90 days, 3 in both groups).

Ischemic Stroke

Trials in patients with an acute ischemic stroke are divergent in the recruitment of study participants, such as the time window after stroke or the use of arterial mechanical thrombectomy. The Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED) enrolled patients with a very acute ischemic stroke within 6 hours, and the other 3 trials enrolled patients with an acute ischemic stroke within 12 or 48 hours after successful reperfusion by arterial mechanical thrombectomy.

The China Antihypertensive Trial in Acute Ischemic Stroke (CATIS) enrolled 4,071 patients with an acute ischemic stroke within 48 hours of onset and elevated systolic blood pressure (140–219 mm Hg) to investigate whether blood pressure reduction (targeting systolic blood pressure for a reduction by 10% to 25% within the first 24 hours after randomization and to 140/90 mm Hg within 7 days) would prevent death and disability (modified Rankin Scale ≥ 3) at 14 days or at discharge. Mean time from stroke onset to randomization was 15 hours. Mean systolic blood pressure was reduced from 166.7 mm Hg at randomization to

![Figure 3. Effects of achieved systolic blood pressure (SBP, A: 1–24 hours, B: 2–7 days) on score of the modified Rankin Scale at 90 days. Odds ratios and 95% confidence intervals (CI, shaded areas) were estimated using ordinal analyses and were shown according to achieved SBP after adjustment for age, sex, region, time from onset to randomization, the National Institutes of Health Stroke Scale score, volume and location of hematoma, intraventricular extension, and randomized treatment. The reference was achieved systolic blood pressure of 130 mm Hg. Reproduced with permission from reference 73.](image-url)
Blood Pressure Goals in Acute Stroke

144.7 mm Hg (−12.7%) within 24 hours and to 137.3 mm Hg at 7 days after randomization in the antihypertensive treatment group. The corresponding values in the non-antihypertensive treatment control group were 165.6 mm Hg, 152.9 mm Hg (−7.2%) and 146.5 mm Hg, respectively. The between-group differences were 9.1 mm Hg within 24 hours and 9.3 mm Hg at 7 days. The 2 groups did not differ for death and major disability at 14 days or hospital discharge (primary outcome, odds ratio 1.00, \( P = 0.98 \)) nor at 3-month post-treatment follow-up (secondary outcome, odds ratio 0.99, \( P = 0.93 \)).64

The ENCHANTED trial enrolled 2,196 thrombolysis-eligible patients with acute ischemic stroke within 6 hours of stroke onset and elevated systolic blood pressure (≥150 mm Hg) to compare intensive (target systolic blood pressure 130–140 mm Hg within 1 hour) with guideline-based (target systolic blood pressure < 180 mm Hg) blood pressure lowering treatment over 72 hours.65 2,175 of the 2,196 randomized patients actually received intravenous alteplase. Median time from stroke onset to randomization was 3.3 hours. Mean systolic blood pressure over 24 hours was 144.3 mm Hg and 149.8 mm Hg in the intensive and guideline groups, respectively. The primary outcome (functional status at 90 days measured by shift in modified Rankin scale scores) did not differ between the 2 groups (intensive versus guideline-based treatment, odds ratio 1.01, \( P = 0.87 \)). However, fewer patients in the intensive group than in the guideline group had an intracranial hemorrhage (odds ratio 0.75, \( P = 0.01 \)).66 The results of a post hoc analysis of ENCHANTED showed that lower blood pressure variability and lower achieved blood pressure level might be associated with a favorable outcome (Figure 4).74

The early Manipulation of Arterial blood Pressure in Acute ischemic Stroke (MAPAS) trial enrolled 218 patients with an acute ischemic stroke within 12 hours of onset to...
compare three systolic blood pressure ranges during 24 hours (140–160 mm Hg, 161–180 mm Hg, and 181–200 mm Hg).66 With the possible use of vasoactive drugs and fluids to achieve the targets, the median systolic blood pressure in the 3 groups in 24 hours was 153 mm Hg, 163 mm Hg, and 178 mm Hg, respectively. Good outcome, defined as a modified Rankin Scale score 0–2 at 90 days, did not differ between the 3 groups (P = 0.27). Symptomatic intracranial hemorrhage was significantly more frequent in the higher than medium and lower systolic blood pressure range groups (P = 0.048).66

The BP-TARGET trial enrolled 423 patients with an acute ischemic stroke that was attributable to a large-vessel occlusion and had successfully reperfusion with endovascular therapy to assess whether an intensive systolic blood pressure target (100–129 mm Hg) would result in a lower rate of intraparenchymal hemorrhage than a standard systolic blood pressure target (130–185 mm Hg).67 The target systolic blood pressure had to be achieved within 1 hour after randomization and maintained for 24 hours with intravenous blood pressure lowering agents. The mean systolic blood pressure during the first 24 hours after reperfusion was 128 mm Hg and 138 mm Hg in the intensive and standard target groups, respectively. The 2 groups were not significantly different for the primary outcome (the rate of radiographic intraparenchymal hemorrhage at 24–36 hours, intensive versus standard treatment, odds ratio 0.96, P = 0.84) nor the primary safety outcome (the occurrence of hypotension) or mortality within the first week after randomization.68

Mixed Hemorrhagic and Ischemic Stroke

Four trials included both patients with an acute hemorrhagic stroke and those with an acute ischemic stroke in acute or subacute phase (within 30 to 72 hours of onset).68–71 Of these 4 trials, 2 compared certain antihypertensive drugs with placebo.68,70 1 compared continuation and discontinuation of antihypertensive drug treatment,69 and 1 compared intensive with standard blood pressure lowering target.71

The controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial was a placebo-controlled double-blind pilot study.68 It enrolled 179 patients with cerebral infarction or cerebral hemorrhage within 36 hours of onset and elevated systolic blood pressure (>160 mm Hg) to receive oral or intravenous labetalol, oral or sublingual lisinopril, or placebo. The doses were titrated up to achieve the target systolic blood pressure (145–155 mm Hg or a reduction of 15 mm Hg from baseline). There was a significantly greater fall in systolic blood pressure within the first 24 hours in the active treatment groups than the placebo group (21 vs. 11 mm Hg). The primary outcome (death or dependency at 2 weeks) was not different between the 2 groups (treatment vs. placebo, relative risk 1.03, P = 0.82). Active treatment did not increase the risk of early neurological deterioration (P = 0.76), but tended to reduce 3-month mortality compared with placebo (hazard ratio 0.40, P = 0.05).68

The Continue or Stop Post-Stroke Antihypertensives Collaborative Study (COSSACS) enrolled 763 patients who were taking antihypertensive drugs and had a stroke within 48 hours of onset to compare continuation with discontinuation of pre-existing antihypertensive drugs for 2 weeks.69 Systolic/diastolic blood pressure at 2 weeks was on average 13/8 mm Hg lower in the continuation than discontinuation group. The continuation and discontinuation groups were not different for the primary endpoint (death or dependency at 2 weeks, a modified Rankin scale score > 3 points, continuation vs. discontinuation, relative risk 0.86, P = 0.3) nor serious adverse events, 6-month mortality, or major cardiovascular events.69

The Scandinavian Candesartan Acute Stroke Trial (SCAST) enrolled 2,029 patients with an acute stroke within 30 hours of onset and elevated systolic blood pressure (≥140 mm Hg) to be treated with either candesartan or placebo for 7 days, with doses increasing from 4 mg on day 1 to 16 mg on days 3 to 7.70 The mean systolic/diastolic blood pressures at 7 days of treatment were 147/82 mm Hg and 152/84 mm Hg in the candesartan and placebo groups, respectively. During 6 months follow-up, the 2 groups had similar risks of the composite vascular endpoint (candesartan vs. placebo, hazard ratio 1.09, P = 0.52), but the candesartan group had a higher risk of poor outcome than the placebo group (odds ratio 1.17, P = 0.048).70

The Controlling Hypertension After Severe Cerebrovascular Event (CHASE) trial enrolled 483 patients with an acute severe (a Glasgow Coma Scale score ≤ 12 or a National Institutes of Health Stroke Scale score ≥ 11) stroke within 72 hours of onset and elevated systolic blood pressure (150–210 mm Hg) to compare a so-called individualized (10–15% reduction in systolic blood pressure from admission achieved within 2 hours and maintained for a week) with a standard systolic blood pressure lowering group (target < 200 mm Hg in acute ischemic stroke and < 180 mm Hg in intracerebral hemorrhage).71 Mean values of systolic blood pressure in the individualized and standard treatment groups were 151.6 mm Hg (12.9% reduction from baseline) and 160.7 mm Hg (6.3% reduction from baseline), respectively, at 2 hours, 144.0 mm Hg (17.0% reduction from baseline) and 148.2 mm Hg (13.3% reduction from baseline), respectively, at 24 hours, and 138.1 mm Hg (20.5% reduction from baseline) and 139.7 mm Hg (18.1% reduction from baseline), respectively, at 7 days. The primary outcome (the proportion of patients with a poor functional outcome at day 90 of enrolment) was non-significantly lower in the individualized than standard treatment group (odds ratio 0.75; P = 0.22).71

CONCLUSIONS AND PERSPECTIVES

Current guideline recommendations on the blood pressure goals in acute stroke are clinically empirical and generally rather conservative. Antihypertensive treatment is recommended only in severe hypertension. Observational studies showed that the relationship between blood pressure and unfavorable clinical outcomes was probably positive in acute hemorrhagic stroke but J- or U-shaped in acute ischemic stroke with undetermined nadir blood pressure. The results of randomized controlled trials are promising
for blood pressure management in hemorrhagic stroke but less so in ischemic stroke. A systolic blood pressure goal of 140 mm Hg is probably appropriate for acute hemorrhagic stroke. The blood pressure goal in acute ischemic stroke, however, remains uncertain, and probably depends on the time window of treatment and the use of revascularization therapy.

Further research is required to investigate the potential benefit of antihypertensive treatment in acute stroke. When such trials are designed, the time window is of paramount importance. In the very early phase of acute stroke, blood pressure variability might be even more important than blood pressure level. Future studies may address whether it is possible to treat increased blood pressure variability and whether such treatment confers any outcome benefit. In the subacute phase of a stroke, blood pressure lowering might be more likely beneficial with a very intensive blood pressure goal, such as, for instance, 130/80 mm Hg.

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