Managing Hypertension in Patients With Acute Stroke

Michael N. Cocchi, MD*; Jonathan A. Edlow, MD

*Corresponding Author. E-mail: mcocchi@bidmc.harvard.edu, Twitter: @MichaelCocchiMD.

INTRODUCTION

For patients presenting to the emergency department (ED) with acute stroke, treatments in the minutes to hours after the event can affect outcomes. Patients with acute stroke often present with elevated blood pressure, which can exacerbate the underlying pathology and drive therapeutic interventions. This article focuses on the current evidence-based approach to blood pressure management in the setting of acute stroke, including acute ischemic stroke, aneurysmal subarachnoid hemorrhage, and intraparenchymal hemorrhage. When direct evidence is lacking, we suggest approaches based on what data do exist, pathophysiologic principles, and our own practice. Table 1 provides a concise summary of existing recommendations and targets based on cause.

GENERAL PRINCIPLES

Elevated blood pressure in the setting of acute stroke is common. In one national data set of greater than 500,000 patients presenting to the ED with stroke, nearly 60% had elevated blood pressure.1 Another systematic review of 18 studies found that 52% of patients with acute stroke were hypertensive at admission.2

Acute blood pressure management in the setting of acute intracranial pathology centers around the principle of optimizing cerebral perfusion pressure, which can be affected by both the mean arterial blood pressure and the intracranial pressure, as represented by the following formula: cerebral perfusion pressure = mean arterial blood pressure–intracranial pressure. As the intracranial pressure increases, the mean arterial blood pressure must be maintained at a level that ensures adequate cerebral perfusion pressure. Autoregulation is the physiologic process by which blood flow in a given circulation (in this case, cerebral) is maintained over a wide range of systemic blood pressure. When autoregulation is intact, cerebral blood flow is maintained in a normal range through vasoconstriction and vasodilation of intracranial vessels. Because the majority of these patients will not have intracranial pressure monitoring, judgments about elevated intracranial pressure are based on clinical (eg, headache, confusion, vomiting, diplopia) or imaging (obliteration of normal cerebral spinal fluid-filled spaces on computed tomography or optic nerve sheath diameter by ultrasonography) findings.

Cerebral perfusion pressure can be manipulated by either decreasing intracranial pressure or increasing mean arterial blood pressure. Elevating the head of the bed to at least 30 degrees is appropriate in most cases when the intracranial pressure is elevated. Given available data and guidelines,3,4 in most cases it is reasonable to maintain the head elevated at 30 degrees, but individual circumstances may be relevant. For example, a patient with acute ischemic stroke and a flow-limiting stenosis may benefit from flat positioning, whereas an intracerebral hemorrhage patient with known elevated intracranial pressure will need head-of-bed elevation. Care should also be taken to avoid reductions in venous return from the head (tight cervical collars or central line dressings) that could elevate intracranial pressure.

In regard to manipulations of mean arterial blood pressure, use of short-acting intravenous agents to manage blood pressure and continuous infusions that can be carefully titrated may be advantageous in the acute setting (Table 2).

Acute Ischemic Stroke

The optimal blood pressure management strategy in acute ischemic stroke remains controversial, in part because of a lack of clear evidence based on randomized controlled trial data. Balancing preservation of perfusion to the cerebral ischemic (but not yet infarcted) penumbra to avoid extension of the infarct with the risk of hemorrhagic conversion is the goal, both of which can result in worsened neurologic outcomes.
For acute ischemic stroke, blood pressure targets will be determined by whether the patient is eligible for treatment with systemic thrombolysis. For acute ischemic stroke patients not undergoing intravenous alteplase or endovascular therapy, there is a 2018 Class IIb American Heart Association (AHA)/American Stroke Association (ASA) position that states that it is reasonable for patients with blood pressure greater than 220/120 mm Hg to experience a decrease in blood pressure of 15% within the first 24 hours after acute ischemic stroke. The data on which the recommendation is made are limited because these patients have been excluded from clinical trials evaluating blood pressure lowering after acute ischemic stroke, so clinical judgment will be necessary, and treatment should be individualized. In patients with various comorbid conditions, such as acute coronary syndrome or heart failure, the decisionmaking involved in blood pressure management may be driven by these other conditions.

### Table 1. Guideline-recommended blood pressure targets.

<table>
<thead>
<tr>
<th>Stroke Type</th>
<th>Target, mm Hg</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute ischemic stroke</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV tPA eligible^5</td>
<td>&lt;185/110</td>
<td>AHA/ASA recommendations are to monitor BP every 15 min for 2 h, then every 30 min for 6 h, and then hourly until 24 h.</td>
</tr>
<tr>
<td>During/after tPA^5</td>
<td>&lt;180/105</td>
<td></td>
</tr>
<tr>
<td>No tPA^5</td>
<td>&lt;220/120</td>
<td></td>
</tr>
<tr>
<td>Mechanical thrombectomy^5</td>
<td>BP ≤180/105</td>
<td>Maintain this range during and for 24 h after the procedure.</td>
</tr>
<tr>
<td><strong>Aneurysmal subarachnoid hemorrhage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unsecured^16</td>
<td>SBP &lt;160</td>
<td>Some experts advocate &lt;140 mm Hg; other recommendations include mean arterial blood pressure &lt;110 mm Hg, SBP &lt;160 mm Hg, or both, or SBP target of &lt;180 mm Hg.</td>
</tr>
<tr>
<td>Secured</td>
<td>Unclear</td>
<td>May depend on patient-specific factors such as premorbid blood pressure and presence of vasospasm.</td>
</tr>
<tr>
<td><strong>Intraparenchymal hemorrhage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial SBP 150 to 220 mm Hg^21</td>
<td>Aim for SBP &lt;140 mm Hg</td>
<td></td>
</tr>
<tr>
<td>Initial SBP &gt;220 mm Hg^21</td>
<td>Aim for SBP 140–160 mm Hg</td>
<td></td>
</tr>
</tbody>
</table>

^IV, Intravenous; BP, blood pressure; SBP, systolic blood pressure.

### Table 2. Commonly used medications for blood pressure management in acute stroke.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Typical Dose/Range</th>
<th>Notes</th>
<th>Cautions/Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>10–20 mg IV during 1–2 min; may repeat 1 time</td>
<td>Onset of action 5 min</td>
<td>Avoid use in COPD, asthma, heart failure, bradycardia, heart block</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>IV infusion at 5 mg/h; titrate up by 2.5 mg/h every 5–15 min; maximum 15 mg/h</td>
<td>Onset of action 1–5 min</td>
<td>Avoid in severe aortic stenosis</td>
</tr>
<tr>
<td>Clevidipine</td>
<td>1–2 mg/h IV; titrate by doubling the dose every 2–5 min until desired BP reached; maximum 21 mg/h</td>
<td>Onset of action 2–4 min; short half-life</td>
<td>Do not use in patients with egg/soy allergy because of lipid emulsion carrier</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Avoid in severe aortic stenosis</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>10–20 mg IV; repeat every 4–6 h</td>
<td>Onset of action 10–20 min</td>
<td>Can cause reflex tachycardia</td>
</tr>
<tr>
<td>Other agents (eg, enalaprilat, esmolol)</td>
<td>may also be considered</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

COPD, Chronic obstructive pulmonary disease.
Current AHA/ASA guidelines suggest that decreasing the blood pressure by 15% in these scenarios is probably safe (Class I). It is important to understand that overtreatment (decreasing the blood pressure too much) risks worsening cerebral ischemia, and this should be considered when medications are titrated. In the China Antihypertensive Trial in Acute Stroke, 4,071 patients who presented within 48 hours of onset of an acute ischemic stroke, with an elevated blood pressure between 140 and 220 mm Hg, were randomized to either antihypertensive treatment (decreasing by 10% to 25% within the first 24 hours after randomization to achieve less than 140/90 mm Hg within 7 days and maintaining that throughout the hospitalization) or the control arm (not receiving antihypertensive treatment, including discontinuation of home antihypertensive medications). There was no significant difference in primary outcome composite measure of death or major disability at day 14 or hospital discharge between groups.

For patients who are potentially eligible for treatment with intravenous alteplase, the systolic blood pressure should be maintained at less than 185 mm Hg and the diastolic blood pressure at less than 110 mm Hg (Class I ASA/AHA recommendation). During or after infusion of a thrombolytic agent, the recommendation is to maintain blood pressure at less than 180/105 mm Hg. The exact blood pressure at which the risk of hemorrhage increases in the setting of systemic thrombolysis is currently unknown and may differ from patient to patient. In the absence of new and more compelling data, it is reasonable to use the blood pressure parameters used in the original trials.

For patients who are undergoing mechanical thrombectomy, there are very limited data about the optimal blood pressure targets during and after the procedure; there is a new Class IIa recommendation for maintaining the blood pressure at less than or equal to 180/105 mm Hg during and for 24 hours after the procedure. In the Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke trial, patients with a proximal intracranial occlusion in the anterior circulation up to 12 hours after onset were randomized to standard care alone versus standard care plus endovascular therapy (mechanical thrombectomy); that protocol advised maintaining systolic blood pressure at greater than 150 mm Hg to maintain flow through collateral vessels, and then in the postprocedure period aiming for a target that would be considered normal for the individual patient. The Diffusion-Weighted Imaging or Computerized Tomography Perfusion Assessment With Clinical Mismatch in the Triage of Wake-up and Late Presenting Strokes Undergoing Neurointervention With Trevo trial, which randomized patients with an occlusion of the intracranial internal carotid artery, the first segment of the middle cerebral artery, or both, and mismatch between clinical deficit severity and infarct volume, to thrombectomy plus standard care versus standard care alone, recommended maintaining systolic blood pressure at less than 140 mm Hg in the first 24 hours after reperfusion from mechanical thrombectomy.

There are no data to favor one agent over another for decreasing blood pressure after acute ischemic stroke. The most common choices are titratable infusions such as nicardipine or clevidipine, but bolus dosing of agents such as labetalol is also reasonable (Table 2). Although not specific to stroke, a 2011 multicenter randomized controlled trial compared use of nicardipine infusion versus labetalol bolus dosing for undifferentiated hypertensive emergency in 226 patients and found that patients who received nicardipine were 2.7 times more likely to be in target blood pressure range within 30 minutes compared with those treated with labetalol. In this trial, overshooting of blood pressure targets was less than 15% with either medication, and no evidence of significant harm was found with either agent. In the absence of compelling evidence of superiority, clinicians may need to consider resources available, as well as other patient-specific parameters such as pulse rate, when deciding on the agent to use. In most cases, we generally prefer nicardipine or clevidipine for blood pressure management when necessary in acute ischemic stroke, given the ease of titration with these agents.

### Aneurysmal Subarachnoid Hemorrhage

The most feared complication of an aneurysmal subarachnoid hemorrhage is rebleeding, which may have an incidence of up to 15% within the first 24 hours and carries with it significant morbidity and mortality, with a fatality rate as high as 70% described. Despite recognition of risk of this complication, evidence supporting a specific blood pressure management strategy that can reduce this danger is limited, and there remains large variability in blood pressure targets used in this subset of intracerebral hemorrhage. In one survey study of 128 clinicians (mostly neurointensivists), systolic blood pressure targets ranged from 140 to 180 mm Hg before aneurysm securement and 160 to 240 mm Hg postsecurement. The current AHA/ASA guidelines suggest a target of systolic blood pressure less than 160 mm Hg before aneurysm securement (Class IIa, Level of Evidence C), whereas the Neurocritical Care Society consensus recommendations endorsed a target of
mean arterial blood pressure less than 110 mm Hg, systolic blood pressure less than 160 mm Hg, or both. European guidelines have been more liberal, with a systolic blood pressure target of less than 180 mm Hg.

Given the paucity of data for specific targets, there is even less guidance on specific agents to achieve blood pressure control in this population. As with patients with acute ischemic stroke, use of easily titratable agents may be preferred, and we generally prefer nicardipine or clevidipine.

**Intracerebral Hemorrhage**

For patients presenting with an intracerebral hemorrhage not related to an aneurysm or other vascular malformation, the focus is on blood pressure management, with a concern for worsening the hemorrhage, although the evidence for particular targets is limited. Hematoma growth is a predictor of morbidity and mortality after intracerebral hemorrhage, and elevated blood pressure in this context has been associated with hematoma enlargement.

The majority of these patients will not have intracranial pressure monitoring devices, and therefore accounting for elevations in intracranial pressure must be made on clinical and neuroimaging factors. In accordance with the most up-to-date 2015 guidelines from the AHA/ASA, for patients who present with a systolic blood pressure 150 to 220 mm Hg without a clear contraindication for acute blood pressure treatment, immediate reduction to 140 mm Hg is likely safe (Class I; LOE A) and may improve functional outcome (Class IIa; LOE B). For patients with systolic blood pressure greater than 220 mm Hg, reduction in the blood pressure with a titratable infusion and frequent blood pressure monitoring is recommended, with a target of systolic blood pressure 140 to 160 mm Hg (Class IIb; LOE C).

Data from recent trials support these recommendations. The Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage trial, a randomized pilot study of 204 patients who presented with intracerebral hemorrhage, demonstrated that rapid reduction to a target of systolic blood pressure 140 mm Hg within 6 hours was safe.

In this trial, the authors also found that there was a reduction in hematoma growth in the intensive target group, although this did not achieve statistical significance. The follow-up trial randomized 2,839 patients with acute intracerebral hemorrhage and elevated blood pressure to either intensive blood pressure management (systolic blood pressure ≤140 mm Hg within 1 hour) or more standard blood pressure management (systolic blood pressure ≤180 mm Hg) and found no difference in mortality, severe disability, or adverse events. In a secondary analysis, the authors identified improvement in functional outcomes as measured by modified Rankin Scale scores in the more intensive control group. The Antihypertensive Treatment of Acute Cerebral Hemorrhage II trial was a randomized controlled trial of 1,000 patients presenting with intracerebral hemorrhage that compared an intensive blood pressure range of systolic blood pressure 110 to 139 mm Hg with a more standard-care range of systolic blood pressure 140 to 179 mm Hg; this trial was stopped early for futility according to a prespecified interim analysis that demonstrated no difference in mortality or disability between the groups. There were more renal adverse events noted in the intensive treatment group.

Guidelines offer a data-driven framework to make decisions, but by necessity, they suggest general approaches to individual patients. Target blood pressure goals should be tailored to individual patients, accounting for baseline premorbid blood pressure levels, the likelihood of elevated intracranial pressure, and comorbid conditions. When appropriate, intracranial pressure monitoring allows clinicians to more rationally decide on a target blood pressure for the individual patient.

**VASOACTIVE MEDICATIONS**

Choice of agent used to manage blood pressure in the acute stroke setting may be based on patient-specific factors, and clinical judgment in the overall context of the patient scenario is important. Using a titratable infusion such as nicardipine or clevidipine may be preferable to a bolus-dosing agent to more carefully achieve the desired response. In a small (n=54) pseudorandomized trial of nicardipine versus labetalol, patients who received nicardipine had more effective blood pressure management and demonstrated a more reliable dose response.

Clevidipine, which is notable for its rapid onset of action and short half-life, has demonstrated efficacy in achieving target blood pressure in spontaneous intracerebral hemorrhage. In general, nitroprusside is avoided in neurocritically ill patients because of its potential to increase intracranial pressure. Regardless of the agent used, it is important to monitor the response closely and avoid inadvertent hypotension.

**SUMMARY**

Optimal blood pressure targets in the setting of acute ischemic stroke, acute subarachnoid hemorrhage, and spontaneous intracerebral hemorrhage remain somewhat controversial, and the evidence is evolving. Guidelines offer a data-driven framework to make decisions, but by necessity, they suggest general approaches to individual
patients. Target blood pressure goals should be informed by existing evidence-based guidelines but tailored to individual patients.

**Supervising editor:** Steven M. Green, MD. Specific detailed information about possible conflict of interest for individual editors is available at [https://www.annemergmed.com/editors](https://www.annemergmed.com/editors).

**Author affiliations:** From the Department of Emergency Medicine (Cocchi, Edlow) and Department of Anesthesia Critical Care, Division of Critical Care (Cocchi), Beth Israel Deaconess Medical Center, Boston, MA.

**Authorship:** All authors attest to meeting the four ICMJE.org authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Funding and support:** By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

**REFERENCES**


