Blood Pressure Management in Acute Stroke

Victor C. Urrutia, MD*, Robert J. Wityk, MD

Cerebrovascular Division, Department of Neurology, Johns Hopkins University School of Medicine, Phipps 126, 600 North Wolfe Street, Baltimore, MD 21287, USA

The optimal management of arterial blood pressure in the setting of an acute stroke has not been defined [1,2]. Many reviews have been published on this topic in the past few years, but definitive evidence from clinical trials continues to be lacking [3–7]. This situation is complicated further because stroke is a heterogeneous disease. The best management of arterial blood pressure may be different depending on the type of stroke (ischemic or hemorrhagic) and among the subtypes of ischemic or hemorrhagic stroke [1,8]. This article reviews the relationship between arterial blood pressure and the pathophysiology specific to ischemic stroke, primary intracerebral hemorrhage (ICH), and aneurysmal subarachnoid hemorrhage (SAH), elaborating on the concept of ischemic penumbra and the role of cerebral autoregulation. The article also examines the impact of blood pressure and its management on outcome. Finally, an agenda for research in this field is outlined.

Cerebral autoregulation

Cerebral autoregulation is the mechanism by which cerebral blood flow (CBF) remains constant across a wide range of cerebral perfusion pressures (CPP). This is achieved by reflex vasoconstriction or vasodilation of the cerebral arterioles in response to changes in perfusion pressure. CPP is defined by the following relationship:

\[ \text{CPP} = \frac{\text{MAP}}{C_0} - ICP \]

Where MAP is mean arterial pressure, and ICP is intracranial pressure. If ICP is constant and not elevated, MAP and CPP are proportional; they can be used interchangeably when talking about autoregulation.
CBF is determined by CPP and cerebrovascular resistance (CVR). CVR is governed primarily by arteriolar diameter, although larger vessels also may contribute. To maintain a constant CBF of approximately 50 mL/100 g/min, CVR responds to CPP by arteriolar vasoconstriction if there is an increase in CPP and arteriolar dilation if the CPP decreases. The autoregulatory system in the brain can maintain essentially constant CBF between a MAP of 50 to 60 mm Hg to 150 to 160 mm Hg. When MAP decreases to less than 50 to 60 mm Hg, maximum vasodilation is reached, and CBF decreases proportionally with the MAP, resulting in ischemia. On the other extreme, when MAP exceeds 150 to 160 mm Hg, arteriolar vasoconstriction is exhausted, and there is continuous increase in hydrostatic pressure that results in cerebral edema and breakdown of the blood-brain barrier (ie, hypertensive encephalopathy or intracerebral hemorrhage) (Fig. 1). There is first segmental vasodilation or sausage-string appearance of the arteries, followed by massive cerebrovascular dilation [9].

In chronically hypertensive individuals, the autoregulation curve is shifted as a result of the elevated MAP levels; the lower and upper limits are higher than in normal individuals. A normal CBF and oxygen consumption are maintained at the expense of a marked increase in the cerebrovascular resistance [9]. These changes result in a decreased tolerance for relative hypotension, as the capacity to maintain a constant CBF at the lower end of the blood pressure spectrum is impaired.

There is evidence that autoregulation is dysfunctional after a stroke. If there is no capacity for autoregulation, CBF increases or decreases

![Diagram of Arteriole Diameter](image_url)

**Fig. 1.** CBF remains constant across a wide range of CPP owing to cerebral autoregulation. This is achieved primarily through arteriolar vasoconstriction and vasodilation in response to changes in CPP. (Adapted from Rose JC, Mayer SA. Optimizing blood pressure in neurological emergencies. Neurocrit Care 2004;3:287–300; with permission.)
proportionally to the MAP, exposing the brain to ischemia from hypoperfusion or edema and hemorrhage in the case of hypertension (Fig. 2). Eames and colleagues [10] measured dynamic cerebral autoregulation by analyzing beat-to-beat, spontaneous blood pressure variability and CBF velocities with transcranial Doppler in 56 stroke patients and 56 matched controls. Global impairment in dynamic autoregulation was found in stroke patients and not in controls. This dysfunction occurred not only in the hemisphere ipsilateral to the infarct, but also contralaterally [10,11].

**Ischemic penumbra**

CBF in the area of a cerebral infarction is not homogeneous. In animal experiments, Astrup and colleagues [12] showed a critical threshold of CBF below which neurons cease to function, but continue to survive for a time. These neurons potentially can return to a normal functional state with restoration of blood flow. Jones and colleagues [13] replicated these findings and suggested that the time window in which ischemia is reversible is in the range of several hours. The current concept of the ischemic penumbra is a region of brain with a gradient of depressed CBF. Tissue with the lowest CBF would be irreversibly damaged and constitutes the core of the infarct [14,15]. The regions surrounding the core, the “penumbra” (Fig. 3), are ischemic and dysfunctional, but potentially salvageable. The length of time during which tissue in the ischemic penumbra survives is controversial, but is likely to depend on the location of cerebral vessel occlusion, the rapidity of occlusion, and the adequacy of collateral blood flow [14].

Fig. 2. In chronic hypertension, the autoregulatory curve is “shifted” to the right, maintaining constant CBF at higher CPP than normal and resulting in a decreased tolerance to relative hypotension. In the setting of cerebral ischemia, autoregulation is impaired, and CBF becomes proportional to CPP. (Adapted from Rose JC, Mayer SA. Optimizing blood pressure in neurological emergencies. Neurocrit Care 2004;3:287–300; with permission.)
With timely reperfusion, the region of ischemic penumbra may be rescued from infarction. This hypothesis also suggests that blood pressure reduction in the setting of acute ischemic stroke may worsen hypoperfusion of the penumbra and hasten extension of the infarct [16].

It has been suggested that MRI diffusion-weighted and perfusion-weighted imaging (DWI and PWI) constitutes a clinically useful analogy to the concept of ischemic penumbra. According to this view, DWI reveals areas of cerebral injury developing within minutes to hours after onset of ischemia; although reversible in exceptional circumstances, the DWI lesion represents for practical purposes the core of the infarct. PWI uses tracking of a bolus of gadolinium to generate relative CBF maps and can indicate regions of hypoperfusion. The subtraction of PWI and DWI volumes—the diffusion-perfusion mismatch—can be operationally used as a representation of the ischemic penumbra (Fig. 4) [17].

**Ischemic stroke**

*Natural history of blood pressure after ischemic stroke*

Increased blood pressure is common in patients presenting with acute stroke, particularly in patients with preexisting hypertension [18]. In most cases, blood pressure spontaneously declines in the first few days after stroke onset, but a significant decline can be seen even in the first few hours after onset in about a third of patients [19]. Numerous studies have examined the relationship between admission blood pressure or early changes in blood pressure and outcome after stroke [20–27]. These studies are contradictory. Some studies note an association of poor outcome with patients with high blood pressure on hospital admission [20,25]. Others have noted a decreased
risk of neurologic deterioration from stroke with higher blood pressure [22] and worse outcomes in patients who have a decrease in blood pressure after admission [24]. The argument can be made that a higher blood pressure may reflect greater stroke severity, rather than causing worse outcomes [28]. Mattle and colleagues [27] reported that there was a greater spontaneous decrease in blood pressure after admission in patients who recanalized after intra-arterial thrombolysis compared with patients with inadequate recanalization. Semplicini and colleagues [29] found that 77% of patients had an elevated blood pressure on admission and noted that in patients with lacunar, large artery atheroembolic and cardioembolic strokes, higher blood pressures (systolic blood pressures [SBP] of 140–220 mm Hg and diastolic blood pressures [DBP] of 70–110 mm Hg) were associated with a better prognosis.

The International Stroke Trial, evaluating more than 17,000 patients, showed a “U-shaped” relationship between blood pressure and mortality, with very low or very high admission blood pressures linked to poor outcome [30]. In the first 48%, 54% of the patients had a SBP greater than 160 mm Hg. It was found that for every increase of SBP of 10 mm Hg over 150 mm Hg, there was an increase in early mortality of 3.8%, and for every decrease of 10 mm Hg below SBP of 150 mm Hg, there was an

Fig. 4. An example of DWI and PWI MRI mismatch and the concept of “penumbra.” On the images labeled as “before Rx,” there is a marked mismatch between a small DWI lesion (brighter signal) and a large area of hypoperfusion in PWI (darker signal). The area of hypoperfusion decreases after treatment with induced hypertension (“during Rx”), whereas the DWI lesion remains the same.
increase in mortality of 17.9% [30,31]. These findings subsequently were replicated in a hospital-based stroke registry [32].

These studies show a physiologic relationship between acute stroke and elevation of blood pressure. It can be argued that in some patients elevated blood pressure may be a marker of stroke severity and not causally related to worse outcomes. It has been postulated that patients with a significant ischemic penumbra may benefit from a higher blood pressure. Loss of autoregulation in ischemic brain may provide an opportunity to manipulate blood pressure to therapeutic ends. Studies evaluating the role of blood pressure modification (elevating or lowering it) in acute ischemic stroke are presented in the next section.

Modifying blood pressure in acute stroke

Blood pressure reduction

Only a few studies have examined the effect of blood pressure reduction in patients with acute ischemic stroke [33–36]. In a Cochrane Review, five trials with a total of 218 subjects were identified [37]. The data were deemed insufficient to make a recommendation on lowering or elevating blood pressure in acute stroke. The American Stroke Association guidelines suggest that, in most cases, there is no imperative to lower blood pressure in the acute setting [1,2]. Numerous case reports and series describe neurologic worsening with excessive blood pressure lowering [38,39].

The Intravenous Nimodipine West European Trial (INWEST) [40] was designed to test whether nimodipine had a neuroprotective effect in stroke. The target population was 600 subjects, but the trial was stopped after recruiting 295 subjects because of an imbalance in the outcomes showing worse outcomes in the groups treated with nimodipine. There were three treatment groups: placebo (n = 100), nimodipine 1 mg/h (n = 101), and nimodipine 2 mg/h (n = 94). Patients were randomly assigned within 24 hours of stroke. SBP decreased by 2.1% from baseline in the placebo group and 6.6% and 11.4% for the low-dose and high-dose nimodipine groups. DBP also decreased by 1.7% in the placebo group and 7.7% and 14.4% in the low-dose and high-dose nimodipine groups. Ahmed and colleagues [35] reanalyzed the data and found that the poorer outcome in the nimodipine groups was associated with lowering of blood pressure, even after adjusting for known risk factors for poor outcome. The acute Candesartan Cilexetil therapy in stroke Survivors Study (ACCESS) [33] used candesartan cilexetil, an angiotensin type 1 receptor antagonist, in ischemic stroke patients, with a goal of blood pressure reduction of 10% to 15% in the first 24 hours. Patients were included in the study if they had elevated blood pressures, as follows: SBP greater than or equal to 200 mm Hg or DBP greater than or equal to 100 mm Hg within the first 6 to 24 hours or SBP greater than or equal to 180 mm Hg or DBP greater than or equal to 105 mm Hg 24 to 36 hours after stroke onset. Patients with more than 70%
carotid stenosis and older than 85 years of age and patients with a decreased level of consciousness or signs of aortic dissection, acute coronary syndrome, or malignant hypertension were excluded. No significant difference was found in blood pressure between candesartan cilexetil and placebo in the first week or the year of follow-up. This study also was stopped early, owing to significantly better outcomes in the candesartan cilexetil group compared with placebo at 1 year. Mortality was 2.9% and 7.2% ($P = .07$) in the candesartan and placebo groups, and stroke recurrence was 9.8% and 18.7% ($P = .026$) in the candesartan and placebo groups. Functional outcome assessed by the Barthel index at 3 months was not significantly different in either group. This trial suggests that in patients without evolving neurologic deficits, who have relatively elevated blood pressures, treatment with an angiotensin type 1 receptor antagonist may be safe and may improve survival and recurrence of stroke by mechanisms independent of blood pressure reduction.

Blood pressure augmentation

Reports of induced hypertension to treat acute ischemic stroke date back to the 1950s. Shanbrom and Levy [41] reported on two patients (one with an internal carotid artery occlusion and one with basilar artery thrombosis) who had fluctuating neurologic deficits followed by persistent neurologic deterioration. Both showed transient improvement in neurologic function after systemic blood pressure was elevated using intravenous norepinephrine. Farhat and Schneider [42] reported clinical improvement using induced hypertension in four patients with cerebral ischemia secondary to large vessel occlusion from various causes (eg, tumor compression of the internal carotid artery, occlusion of the internal carotid artery for treatment of an intracranial aneurysm). Patients seemed to have a blood pressure threshold below which neurologic deficits returned. Wise [43] reported on induced hypertension in two patients with acute ischemic stroke complicating angiography. In the first patient, induced hypertension was discontinued after 5 hours without recurrence of neurologic deficit. The second patient was treated for 2 days, until he could undergo carotid endarterectomy. Wise and coworkers [44] reported on 13 patients with acute ischemic stroke whose blood pressure was augmented within several hours of onset of symptoms. Fairly rapid clinical improvement (eg, within 1 hour of induced hypertension) was noted in 5 of 13 patients, and improvement was maintained in 3 of 5 patients when assessed 24 hours later. In many of these patients, neurologic deficits seemed to be blood pressure dependent. Deficits returned when hypertensive treatment was stopped and improved again with reinstitution of induced hypertension. Baseline MAP was 65 to 100 mm Hg in the five responders, and a clinical response was seen after MAP elevation of 13 to 30 mm Hg above baseline. No systemic complications were reported. Olsen and coworkers [11] and Agnoli and colleagues [45] examined the
effects of induced hypertension on CBF using intracarotid tracer injection methods. Areas of cerebral hypoperfusion showed partial reperfusion with elevation of systemic blood pressure, confirming the loss of autoregulation in ischemic brain \[11,45\]. Despite these early positive reports, induced hypertension did not achieve widespread use because of the perception of a high risk of ICH and worsening of brain edema.

Several groups have reported on patients with ischemic stroke who were treated with induced hypertension in the neurologic intensive care setting. Rordorf and associates \[46\] reviewed 30 ischemic stroke patients treated with induced hypertension and compared them with 30 similar stroke patients treated with standard therapy. Intravenous phenylephrine was used to increase blood pressure until neurologic deficits improved. Treatment was started within 24 hours of stroke onset and was continued for a mean of 110 hours (range 7–576 hours). Neurologic improvement occurred in 10 of 30 of the treated patients and occurred at an SBP threshold of 130 to 180 mm Hg. Improvements in neurologic deficits occurred 2 to 30 minutes of raising blood pressure. At follow-up, 4 of the 10 patients who responded had no neurologic deficit and no infarct on brain imaging, despite the fact that they had an average of 10 hours of neurologic deficit before improvement. There was no overall difference in neurologic or cardiac complications between the patients treated with or without induced hypertension. In contrast, the nontreatment group had higher rates of ICH and cerebral edema on CT scan. Because this was a nonrandomized, retrospective review, it is possible that CT findings biased patient selection. The same investigators subsequently performed a prospective study of induced hypertension in 13 subjects with acute ischemic stroke within 12 hours of onset of symptoms \[47\]. Exclusion criteria included recent cardiac ischemia, congestive heart failure, intracerebral hemorrhage, or cerebral edema on initial head CT scan. All patients had admission SBP of less than 200 mm Hg. The goal was to increase SBP to at least 160 mm Hg or to 20% above the admission SBP, with a maximum allowed SBP of 200 mm Hg. Neurologic improvement was defined as a reduction by at least 2 points in the National Institutes of Health Stroke Scale performed by two independent examiners. To avoid misinterpretation of spontaneous improvement as treatment-related improvement, phenylephrine was discontinued in all responders. After SBP returned to baseline for 20 minutes, the patient was examined for neurologic deterioration. A beneficial neurologic response was seen in 7 of 13 patients with blood pressure elevation. Induced hypertension therapy was continued for 1 to 6 days and eventually successfully weaned in all patients. In the responders, the neurologic deficit did not worsen between discontinuation of induced hypertension and time of discharge. At the time of discharge, the mean NIHSS was 7.4 (range 2–15) among responders compared with an NIHSS of 10 (range 5–15) among nonresponders. Despite the presence of multiple cardiovascular risk factors in the patients enrolled, there were no cardiac or neurologic complications associated with treatment.
Hillis and colleagues [48,49] used DWI and PWI to study the neural basis of aphasia and cognitive function in acute stroke patients. One patient studied in detail was a 55-year-old, right-handed man with a left carotid artery occlusion who had a left middle cerebral artery territory infarct primarily involving the frontal lobe [50]. Neurologic examination revealed a transcortical motor aphasia with telegraphic speech and frequent paraphasias. DWI revealed a large region of restricted water diffusion in the left frontal lobe, but PWI showed an even larger area of hypoperfusion also involving the anterior left temporal lobe (Wernicke’s area). On serial testing, it was noted that his language ability fluctuated and worsened with a relative decrease in blood pressure. When his MAP was increased from a baseline of 88 mm Hg to a maximum of 100 mm Hg, PWI showed reperfusion of Wernicke’s area, and a marked improvement in word and sentence comprehension was noted. The patient eventually was transitioned from intravenous phenylephrine to oral medications (fludrocortisone, salt tablets, and midodrine) to maintain an elevated MAP. By 2 months after stroke onset, this patient could be tapered off of these oral medications without worsening of aphasia and with return to his normal BP. A repeat PWI at that time showed normal perfusion to Wernicke’s area and no expansion of the infarct beyond the original DWI abnormality. The remarkable feature of this case was that induced hypertension resulted in partial but objective neurologic improvement when started 7 days after onset of stroke. Similar findings subsequently were reported in five other patients treated with induced hypertension 1 to 9 days after ischemic stroke [51].

With this preliminary experience, Hillis and colleagues [52] went on to perform a prospective, unblinded study of induced hypertension in 15 subjects who were randomly assigned in a 2:1 ratio to receive induced hypertension or standard stroke care. Patients were included if they had acute ischemic stroke presenting within 1 and 7 days of onset of symptoms, a quantifiable neurologic deficit, and a diffusion-perfusion mismatch of 20% or greater on baseline MRI scan. Exclusion criteria included recent cardiac ischemia, congestive heart failure, hemorrhage on CT scan, or contraindication to intravenous phenylephrine use. MAP was increased initially by discontinuing antihypertensive medications, then with intravascular volume expansion, and finally with intravenous phenylephrine. MAP was increased in increments of 10% to 20% above baseline with a goal to improve NIHSS by 2 or more points. The maximum allowed MAP was 140 mm Hg. All patients treated with induced hypertension were admitted to the neurologic ICU. Nine patients were randomly assigned to induced hypertension and six to standard care. The two groups were similar in terms of age, baseline NIHSS, and volume of DWI and PWI lesions on baseline MRI scan. By day 3, patients in the induced hypertension treatment arm had a significantly better mean NIHSS (5.6 versus 12.3; \( P < .02 \)) compared with the standard treatment group, and this difference persisted until follow-up at 6 to 8 weeks (mean NIHSS 2.8 versus 9.7; \( P < .04 \)). No patient
in the study experienced a serious adverse event. Six of 9 patients treated with induced hypertension were classified as responders (ie, showed a reduction of >2 points on the NIHSS, which was associated with an increase in MAP between 14 and 27 mm Hg [13–30%]). There was no significant difference in either treatment group in the volume of DWI lesion, whereas patients treated with induced hypertension had a significant reduction in PWI lesion volume (from mean 132 mL to 58 mL; \( P < .02 \)) and a significant reduction in the volume of diffusion-perfusion mismatch (from mean 83 mL to 53 mL; \( P < .005 \)). Independent of treatment, improvements in NIHSS seemed to correlate with a significant reduction in PWI volume on serial scans [53].

Marzan and colleagues [54] used norepinephrine to induce hypertension in 34 ischemic stroke patients, in a study that included patients who would have been excluded from most of the other published investigations [55]. Among the 34 subjects, 14 had infarcts on baseline CT involving greater than one third the middle cerebral artery territory, 8 were concomitantly treated with thrombolytic agents, and 17 received intravenous heparin. Nine of 34 patients (26%) were responders (>2 point improvement in NIHSS); however, among patients not treated with thrombolytic therapy, 5 of 26 (19%) were responders. Serious complications potentially related to induced hypertension occurred in two patients (cardiac arrhythmia and symptomatic intracerebral hemorrhage). The investigators believed this was an acceptable rate of complications, particularly given the severity of stroke and the relative aggressive nature of the interventions. Koenig and colleagues [55] reviewed the outcomes and adverse events associated with use of any form of blood pressure elevation in patients with acute ischemic stroke who had baseline diffusion-perfusion MRI studies and were treated within 7 days of onset of symptoms. Forty-six treated patients were compared with 54 patients from the same time period who received “standard therapy.” Treated patients were more likely to have a larger volume of diffusion-perfusion MRI mismatch and the presence of large artery atherosclerosis and were more likely to be treated in the neurologic ICU. Treated patients had a decrease in median NIHSS by the time of discharge, but this was not statistically significant. Serious adverse events occurred in four patients in each group.

Several other approaches to blood pressure manipulation in stroke patients have been reported. In a study of diaspirin cross-linked hemoglobin (DCLHb), a hemoglobin-based oxygen carrier, in acute stroke patients, a dose-dependent elevation of MAP was noted in the DCLHb-treated subjects [56]. There was no excess of hemorrhagic transformation, cerebral edema, or hypertensive encephalopathy in the treated group. The overall clinical outcome was not improved, however, in the treated patients. Finally, Campbell and associates [57] reported on the use of intra-aortic balloon pumps placed above and below the renal arteries, causing partial aortic obstruction and resulting in increased cerebral perfusion, sometimes with
no systemic blood pressure elevation. Cerebral blood flow as assessed by transcranial Doppler, angiography, or positron emission tomography (PET)/single-photon emission computed tomography (SPECT) improved in 12 of 16 patients.

**Summary: blood pressure and acute ischemic stroke**

Currently, the optimal management of blood pressure in acute stroke remains poorly defined. From a review of the literature, the authors offer the following conclusions: (1) At the onset of acute stroke, there is elevated blood pressure in most patients, and this elevated blood pressure tends to return to normal prestroke levels in approximately 7 days. (2) There is no conclusive evidence to support lowering the blood pressure in acute stroke. There may be a benefit from the early use of angiotensin II type 1 receptor blocking agents, with improvement of long-term (1 year) mortality and stroke recurrence. This benefit was seen despite a lack of a statistically significant blood pressure effect and needs to be confirmed by a larger randomized controlled trial. (3) In selected cases, blood pressure augmentation may be beneficial and safe in the management of acute ischemic stroke. (4) More research is needed to identify effective strategies for blood pressure management in acute ischemic stroke. Clinical trials such as the proposed CHHIPS (Controlling Hypertension and Hypotension Immediately Post-Stroke) may help answer these questions [31]. Until such data are available, the guidelines of the American Heart Association provide a reasonable approach to this problem [1,2].

**Hemorrhagic stroke**

*Intracerebral hemorrhage*

The role of blood pressure management in the acute phase of primary ICH is equally not well defined. Elevated blood pressure is seen in 46% to 56% of patients presenting with ICH [58]. Outcomes after ICH are closely related to hematoma size and hematoma expansion [59,60]. Ohwaki and colleagues [61] studied 76 patients and used a multiple logistic regression model to show that SBP of more than 160 mm Hg was independently associated with hematoma growth. Studies have shown that hematoma expansion occurs very early within the first 24 hours in 38% of patients [62]. The hypothesis has been advanced that lowering the blood pressure in the acute setting may decrease hematoma expansion rate and improve prognosis, yet this remains to be tested in clinical trials. The concept of decreasing blood pressure after ICH has been met by concerns about reducing CBF and promoting ischemia in the perihematomal brain tissue. This has been studied in a few patients using SPECT, PET, and DWI MRI. Recent results suggest that in the acute setting regional CBF is
reduced around the hematoma with a matching decrease in cerebral metabolic rate of oxygen. The oxygen extraction fraction remains low, indicating that there is no region of ischemia [63–65]. Stages of CBF have been proposed in the perihematoma area, as follows [66]:

- **Hibernation**—decreased CBF, decreased cerebral metabolic rate of oxygen, and decreased oxygen extraction fraction (0–48 hours)
- **Reperfusion**—blood flow is heterogeneous and can be decreased, normal, or augmented. (48 hours to 14 days)
- **Normalization** (>14 days)

In a study by Powers and colleagues [64], 14 ICH patients were studied with a baseline PET scan 6 to 22 hours after onset of symptoms. Blood pressure was lowered by 15%, from a MAP of 143 to 119 mm Hg with either nicardipine or labetalol, and repeat PET showed that the CBF remained stable in the perihematomal area. Studies such as this and the one done by Ohwaki and colleagues [61,64] suggest that reducing blood pressure in the first 24 hours after ICH is relatively safe. In a study by Qureshi and coworkers [58], 27 ICH patients were treated to reduce SBP to less than 160 mm Hg and DBP to less than 110 mm Hg. Only 2 of 27 patients deteriorated neurologically, and only 9.1% had hematoma expansion (defined as a growth of the hematoma in >33%).

These data indicate that treatment of hypertension could be beneficial to reduce hematoma expansion and clinical deterioration in the acute period after intracerebral hemorrhage. The Guidelines from the American Stroke Association, published in 1999, recommend maintaining MAP less than 130 mm Hg and, if an ICP monitor is in place, a CPP greater than 70 mm Hg [8]. A large randomized controlled trial is needed to confirm these findings and determine the optimal strategies for blood pressure reduction in ICH.

**Aneurysmal subarachnoid hemorrhage**

Management of aneurysmal SAH is governed by different priorities and paradigms depending on the time after onset of the hemorrhage. SAH occurs in more than 30,000 individuals per year in the United States, and 30-day mortality is 25% to 50% [67]. The biggest concern in the first few days after rupture is rebleeding, which occurs in 9% to 30% of patients. The risk is 20% in the first 2 weeks and 30% in the first months if the aneurysm remains untreated. Mortality in patients who rebleed increases to 50% to 80% [68,69]. After the aneurysm has been secured by clipping or coiling, the next major concern is vasospasm. Symptomatic vasospasm occurs in 30% of patients and is a major cause of morbidity and mortality in SAH. Its incidence peaks between days 10 and 14 after SAH [67]. Blood pressure may be an important determinant of rebleeding and vasospasm.
The risk of rebleeding is highest in the first 24 hours after SAH [68,70]. Ohkuma and colleagues [68] studied 273 patients and found aneurysmal rerupture in 13.6% within the first 24 hours. In the same study, they found that there was a statistically significant higher risk of rebleeding in patients with SBP greater than 160 mm Hg. Claassen and coworkers [71] found, in a group of 467 patients with SAH studied within the first 3 days, that MAP less than 70 mm Hg or greater than 130 mm Hg was an independent predictor of death and disability at 3 months. Hypotension with MAP of less than 70 mm Hg is seen in 4% of all patients with SAH in the acute period, whereas 33% to 50% of patients present with elevated blood pressure. In this study, however, hypertension was not independently associated with rerupture.

In patients within days 1 to 4 of the onset of an SAH and without vasospasm, hydrocephalus, or ICH, PET shows a decrease in cerebral metabolic rate of oxygen, CBF, and cerebral blood volume with normal oxygen extraction fraction. There is a coupled reduction of metabolism and CBF [63]. This is similar to the pattern in the perihematomal region in an intracerebral hemorrhage, discussed earlier. One could postulate, based on the experience with ICH, that there would be no increase in ischemia by lowering blood pressure if the above-mentioned criteria are met.

Early studies of blood pressure management after SAH, which were completed before the adoption of early aneurysm surgery as a standard of care, suggested that patients who benefited from treatment of hypertension to prevent rebleed subsequently had a higher rate of ischemic stroke later in the course when vasospasm was more prevalent [72]. This change in priority as the patient evolves from a situation of high rebleed risk to a high vasospasm risk makes interpretation of these studies difficult. Wijdicks and colleagues [72] studied 134 patients enrolled in a trial of tranexamic acid in which 80 (60%) were treated with antihypertensive medication. Rebleeding occurred in 12 of 80 (15%) patients treated with antihypertensives compared with 18 of 54 patients (33%) who did not receive antihypertensives. Cerebral infarction occurred more often, however, in patients with antihypertensive treatment (34 of 80 patients [43%] versus 12 of 54 patients [22%] without antihypertensives) [72].

There has not been a randomized controlled trial of blood pressure management in early SAH. Data from observational studies suggest a benefit in avoiding the extremes of blood pressure. Also, if there is no vasospasm, hydrocephalus, or ICH with increased ICP, blood pressure reduction may be safe. Based on expert opinion and accumulated experience, it seems reasonable to maintain SBP at less than 160 mm Hg before treatment of the aneurysm, provided that the above-outlined conditions are met [67]. A well-designed randomized controlled trial is needed to address this important question. After definitive aneurysm treatment by clipping or coiling, a strategy of permissive or induced hypertension is commonly implemented to improve CBF in the setting of vasospasm; however, clinical trials also are needed to support this practice.
References


BLOOD PRESSURE MANAGEMENT IN ACUTE STROKE


