



RESEARCH ARTICLE

MANAGEMENT OF ACUTE AND RECURRENT STROKE WITH CONTROL OF BLOOD PRESSURE

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ABSTRACT

Hypertension is the most important modifiable risk factor for stroke. (Gorelick, 2002; Pedelty and Gorelick, 2004) It is estimated that 25% or more of strokes may be attributable to hypertension. Because many patients with stroke have mild hypertension or prehypertension, we have shifted our focus and now think of stroke on a continuum of risk based on blood pressure (BP) level rather than on a threshold effect. (Elliott, 2007) Because high BP may not exist in isolation, a wider definition of hypertension has been proposed that also takes into account the absolute risk of cardiovascular events and associated metabolic factors or early disease markers. (Elliott, 2007)

INTRODUCTION

Lowering BP reduces the risk of stroke. Epidemiological studies have shown that for each 10 mm Hg lower systolic blood pressure (SBP), there is a decrease in risk of stroke of approximately one third in persons aged 60 to 79 years. This association is continuous down to levels of at least 115/ 75 mm Hg and is consistent across sexes, regions, stroke subtypes, and for fatal and nonfatal events. (Lawes *et al.*, 2004) Lowering diastolic blood pressure (DBP) was once the main target to achieve stroke and other cardiovascular event reduction, but SBP has now become the target. (Elliott, 2007) As recently shown, even the elderly with sustained SBP elevation may gain from BP reduction in relation to less fatal or nonfatal stroke, death, and heart failure.5 Although the role of longer-term BP control to improve outcomes in patients with stroke is undisputed, BP management immediately after a stroke remains controversial. In an effort to resolve this controversy, several pilot clinical trials have been initiated. In this review, we discuss the results of some of these trials and available evidence-based guidelines for BP control in the settings of acute ischemic and hemorrhagic stroke (excluding subarachnoid hemorrhage) and in recurrent stroke prevention.

Blood Pressure Management after Intracerebral Hemorrhage:

Patients with Intracerebral Hemorrhage (ICH) often have elevated BP. (Fogelholm *et al.*, 1997) Approximately one third of all patients with ICH presenting within 3 hours of symptom onset have a significant expansion of the hematoma over the next 20 hours. (Brott *et al.*, 1997) Initial hematoma volume and hematoma expansion are powerful predictors of mortality after ICH. (Davis *et al.*, 2006) Some studies have suggested an association between high BP and hematoma expansion and BP is often lowered under the assumption that high BP promotes hematoma expansion. (Ohwaki *et al.*, 2004) However, 2 recent studies question this relationship. In a series of 65 prospectively studied patients with ICH presenting within 3 hours, 37% had significant hematoma enlargement within 24 hours. Neither baseline nor peak BP was significantly associated with hematoma growth. (Jauch *et al.*, 2006) In another pooled analysis of 218 patients with onset of symptoms 3 hours, hematoma volume was measured at presentation and 20 to 24 hours later. Percentage hematoma growth, initial ICH volume, Glasgow Coma Scale score, and presence of intraventricular hemorrhage were all associated with increased mortality; however, BP was not. (Davis *et al.*, 2006) Nonetheless, there may be other reasons to lower BP. Hypertensive patients with ICH may have heart failure or elevated cardiac troponin in which lowering BP might be helpful. (Hays and Dinger, 2006) The argument against lowering BP in acute ICH is based on the possible existence of a perihematomal ischemic zone. Recent studies, however,

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indicate that low blood flow around the hematoma may be a consequence of reduced cerebral metabolism in this area rather than a primary reduction of blood flow. (Zazulia *et al.*, 2001) In addition, chronic hypertensives (due to a shift in the autoregulatory curve) and patients with increased intracranial pressure (ICP; due to lowered cerebral perfusion pressure) may develop cerebral ischemia if BP is acutely lowered.

The Evidence

Previous studies on BP management in ICH have been limited by small sample sizes or retrospective designs. Three prospective pilot trials on acute BP reduction after ICH have recently concluded and the results were presented at the International Stroke Conference in 2015. It should be pointed out that trials were not powered to assess clinical efficacy. The Antihypertensive Treatment of Acute Cerebral Hemorrhage study was a multicenter US study addressing the tolerability and safety of intravenous nicardipine infusion for 18 to 24 hours postictus in patients with ICH with a SBP of 200 mm Hg presenting within 6 hours of symptoms. (Qureshi, 2008) Three SBP goals (170 to 200, 140 to 170, and 110 to 140 mm Hg) were targeted. The study moved to a lower treatment target if there were no safety concerns at the higher target. Fifty-eight patients (18, 20, and 20 in each target group, respectively) with relatively small hematomas (mean volume 20 mL) were enrolled. There was no difference in 3-month mortality between the groups and the safety-stopping rule was not activated in any tier. (Qureshi, 2008) In a larger Asian study, Intensive blood pressure reduction in acute cerebral hemorrhage trial, hypertensive patients (SBP 150 to 220 mm Hg) with an acute ICH within 6 hours of symptom onset were randomized to antihypertensive treatment to a target of 140 mm Hg (intensive group; n203) or 180 mm Hg (guideline group; n201) for 7 days or until hospital discharge. (Anderson *et al.*, 2008) Most of the patients were residents of China (95%), in a good clinical grade (median Glasgow Coma Scale 14) with small deep ganglionic hematomas. Compared with the guideline group, the intensive group showed significantly lower mean proportional hematoma growth at 24 hours (13.7% versus 36.3%; $P=0.04$). However, this difference was not significant after adjustment for initial hematoma volume and time from onset of ICH to CT scan. There was no significant difference in adverse event rate or outcome at 90 days. (Anderson *et al.*, 2008) The Control of Hypertension and Hypotension Immediately Post-Stroke (CHHIPS) pilot trial is discussed subsequently. Notably, this trial included patients with ischemic and hemorrhagic stroke. The small number of patients with ICH (n25) makes interpretation of the results in this stroke subtype quite difficult. (Potter *et al.*, 2009) The results of these 3 trials indicate that intensive BP-lowering in the acute phase is clinically feasible and well tolerated. Larger trials are planned to test the hypothesis that hematoma expansion can be limited by acute treatment of hypertension.

Questions and answers about blood pressure

Management After Acute: Intracerebral Hemorrhage

What Blood Pressure Level Is Considered to Be Too High and Requiring Immediate Reduction?

Answer: Despite absence of definitive supportive evidence, some experts believe that a SBP of 180 mm Hg or a mean

arterial pressure (MAP) of 130 mm Hg would warrant immediate lowering. (Broderick *et al.*, 2007) In the presence of conditions such as acute heart failure, hypertensive encephalopathy, active cardiac ischemia, and so on, lower BP targets may be appropriate.

What Is the Appropriate Target Blood Pressure in Patients With ICH?

Answer: Immediately after an ICH, it is perhaps more appropriate to tailor the target BP to each patient rather than using a "one size fits all" approach. The possibility of increased ICP and a history of chronic untreated hypertension should be considered while choosing the target. Recognizing the absence of definitive data, the American Heart Association/ American Stroke Association (AHA/ASA) guidelines suggest maintaining a cerebral perfusion pressure of 60 to 80 mm Hg in patients with possible increased ICP and a BP of 160/90 or a MAP of 110 mm Hg in other patients. (Broderick *et al.*, 2007) Recent data from pilot trials indicate that a more aggressive BP reduction in patients with relatively small hematomas to normotensive levels soon after an ICH is quite well tolerated. (Qureshi, 2008; Anderson *et al.*, 2008) We await the results of planned larger clinical trials to see if this approach will result in improved outcomes.

Table 1. AHA/ASA Recommendations for BP Management in Acute Cerebral Hemorrhage (Broderick *et al.*, 2007)

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| <ol style="list-style-type: none"> 1. If SBP is 200 mm Hg or MAP is 150 mm Hg, consider aggressive reduction of BP. 2. If SBP is 180 mm Hg or MAP is 130 mm Hg and ICP may be elevated, consider monitoring ICP and reducing BP to keep cerebral perfusion pressure between 60 and 80 mm Hg. 3. If SBP is 180 mm Hg or MAP is 130 mm Hg and there is no evidence of or suspicion of elevated ICP, consider modest BP reduction (eg, MAP of 110 mm Hg or target blood pressure of 160/90 mm Hg). |
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How Fast Should Blood Pressure Be Lowered?

Answer: results of small studies suggest that rapidly lowering MAP by approximately 15% does not lower cerebral blood flow, whereas reductions of 20% can do so. (Powers *et al.*, 2001; Kuwata *et al.*, 1995) Therefore, if BP-lowering is considered, current guidelines suggest cautious lowering of BP by no more than 20% in the first 24 hours. 16, 19

What Antihypertensive Agents Are Appropriate for Use in the Acute Setting?

Answer: Short and rapidly acting intravenous antihypertensive agents are preferred. In the United States, labetalol, hydralazine, esmolol, nicardipine, enalapril, nitroglycerin, and nitroprusside have been recommended. (Broderick *et al.*, 2007) Intravenous urapidil is also used in Europe. (Steiner *et al.*, 2006) Large studies comparing various antihypertensives are not available. Sodium nitroprusside and nitroglycerin should be used with caution because these agents can potentially increase ICP.

Guidelines

In Table 1, we summarize the AHA/ASA guidelines on the management of hypertension in patients with ICH. (Broderick

et al., 2007) The European Stroke Initiative, Canadian Hypertension Education Committee, and the International Society of Hypertension have also published guidelines that are referenced for review. (Steiner *et al.*, 2006; Bath *et al.*, 2003; Boulanger *et al.*, 2005)

Blood Pressure Management After Acute

Ischemic Stroke

An elevated BP, that often declines spontaneously, is seen on presentation in most patients with acute ischemic stroke. (Britton *et al.*, 1986) Several studies have emphasized the effect of elevated BP on outcome after stroke, but the results are inconsistent. (Britton *et al.*, 1986; Okumura *et al.*, 2005) In the International Stroke Trial, the largest of these studies, there appeared to be a U-shaped relationship between BP and mortality. Early death increased by 17.9% for every 10 mm Hg below a SBP of 150 mm Hg and by 3.8% for every 10 mm Hg above a SBP of 150 mm Hg. (Leonardi-Bee *et al.*, 2002)

The Evidence

There is a paucity of clinical trial data addressing BP management in the setting of an acute ischemic stroke. A Cochrane review of 218 patients from 5 clinical trials concluded that the data were insufficient to make a firm recommendation on the value of acute BP reduction after a stroke. (Blood pressure in Acute Stroke Collaboration (BASC), 2001) In the Acute Candesartan Cilexetil Evaluation in Stroke Survivors trial, hypertensive patients with acute stroke (symptom onset 72 hours) treated with Candesartan for 7 days had a significantly improved outcome compared with the placebo group. However, there was no BP difference between the groups and therefore improved outcome cannot be attributed to a direct effect of lowering BP. Moreover, this trial was powered to evaluate the safety rather than the efficacy of acute BP reduction. (Schrader *et al.*, 2003) The CHHIPS pilot trial randomized patients with ischemic or hemorrhagic stroke with a SBP 160 mm Hg to treatment with lisinopril (n58), labetalol (n58), or placebo (n63) within 24 hours (later extended to 36 hours) of symptom onset. The target was a SBP of 145 to 155 mm Hg or a 15 mm Hg fall. Active treatment resulted in a significant difference in SBP without an increase in adverse events compared with placebo. There was no difference in the primary outcome measure with 61% of the active group dead/dependent at 2 weeks compared with 59% of the placebo group. However, there was a borderline significant difference in survival at 90 days (11 deaths in the active group [10%] vs 12 deaths in the placebo group [20%], HR 0.4, 95% CI 0.2–1.0, $P < 0.05$). The results indicate that it is reasonable to proceed with a larger trial to establish the efficacy of acute BP-lowering in improving outcome. (Potter *et al.*, 2009)

Questions and Answers on BP Management

Immediately After an Acute Ischemic Stroke

Should Blood Pressure Be Lowered in Patients With Elevated BP After an Ischemic Stroke?

Answer: As per the AHA/ASA guidelines, it is recommended that before intravenous thrombolytic treatment, BP should be lowered if 185 mm Hg systolic or 110 mm Hg diastolic. After thrombolytic treatment, SBP should be kept 180 mm Hg and

DBP 105 mm Hg. Intravenous labetalol, nitropaste, nicardipine infusion, and, if BP remains elevated, sodium nitroprusside are the recommended agents. (Adams *et al.*, 2007) Despite the absence of supporting evidence, these recommendations are often applied to patients receiving other forms of reperfusion therapy (eg, intra-arterial thrombolysis, clot retrieval, and so on). (Adams *et al.*, 2007) Patients with other indications for BP-lowering such as acute heart failure, aortic dissection, and so on should have the BP lowered. One should be cautious about abruptly lowering BP in other patients due to the risk of worsening cerebral ischemia. (Fischberg *et al.*, 2000) Guidelines suggest withholding antihypertensive agents in these patients unless the DBP is 120 mm Hg or the SBP is 220 mm Hg and limiting the drop in BP during the first 24 hours by approximately 15%. (Adams *et al.*, 2007)

Table 2. AHA/ASA Recommendations for BP Management in Acute Ischemic Stroke (Adams *et al.*, 2007)

1. Patients eligible for treatment with intravenous thrombolytics or other acute reperfusion intervention and SBP 185 mm Hg or DBP 110 mm Hg should have BP lowered before the intervention. A persistent SBP of 185 mm Hg or a DBP 110 mm Hg is a contraindication to intravenous thrombolytic therapy. After reperfusion therapy, keep SBP 180 mm Hg and DBP 105 mm Hg for at least 24 hours.
2. Patients who have other medical indications for aggressive treatment of BP should be treated.
3. For those not receiving thrombolytic therapy, BP may be lowered if it is markedly elevated (SBP 220 mm Hg or DBP 120 mm Hg). A reasonable goal would be to lower BP by approximately 15% during the first 24 hours after onset of stroke.
4. In hypotensive patients, the cause of hypotension should be sought. Hypovolemia and cardiac arrhythmias should be treated and in exceptional circumstances, vasopressors may be prescribed in an attempt to improve cerebral blood flow.

Should Blood Pressure Be Elevated to Improve Cerebral Perfusion in Patients With Ischemic Stroke?

Answer: A few small case series have shown neurological improvement with induced hypertensive therapy. Studies are underway to assess the usefulness of this form of therapy in patients with a diffusion-perfusion mismatch on MRI. (Wityk, 2007) In the meantime, it is reasonable to try volume expansion and/or vasopressors in patients with hypotensive stroke or in patients who have had a worsening of the neurological deficit in association with a drop in BP.

Should Patients on Antihypertensive Agents Have Their Medications Held or Continued?

Answer: There are no substantial clinical data available to answer this question and a clinical trial is underway to address this issue (Continue or stop poststroke anti-hypertensives study). (Lewin, 2008) The AHA/ASA guidelines recommend restarting antihypertensives at 24 hours in previously hypertensive neurologically stable patients unless contraindicated. (Adams *et al.*, 2007)

Guidelines

In Table 2 we summarize AHA/ASA guidelines. (Adams *et al.*, 2007) The European Stroke Organization guidelines are referenced for review. (European Stroke Organisation (ESO) 2008)

Blood Pressure Management and Prevention of Recurrent Stroke

The Evidence

There is substantial evidence to support BP-lowering for prevention of a first stroke; however, few trials have focused on antihypertensive therapy for recurrent stroke prevention. Two recent studies that addressed this issue are Perindopril Protection Against Recurrent Stroke Study (PROGRESS) and Morbidity and Mortality after Stroke, and Eprosartan compared with Nitrendipine for Secondary Prevention study (MOSES). (PROGRESS Collaborative Group, 2001; Schrader *et al.*, 2005) A third trial, Prevention Regimen for Effectively avoiding Second Strokes (PRoFESS), was recently published. (Yusuf *et al.*, 2008) PROGRESS was a well-conceived and conducted clinical trial of BP-lowering. A total of 6105 patients with a history of stroke or transient ischemic attack within the past 5 years were eligible to be randomized to perindopril, an angiotensin-converting enzyme inhibitor with or without indapamide, a thiazide-like diuretic, versus placebo as add-on therapy. In the perindopril-based treatment group, BP was lowered by approximately 9/4 mm Hg, and there was a statistically significant 28% relative risk reduction for the primary outcome, total stroke, as well as other important results in relation to major vascular event reduction. (PROGRESS Collaborative Group, 2001) Overall, with greater lowering of BP, the risk reduction benefit increased for major outcome end points. There has been debate about the value of perindopril alone in reducing major vascular events because BP was only reduced by approximately 5/3 mm Hg in this group corresponding to a 5% nonsignificant reduction in total stroke. A significant reduction of stroke risk was only achieved for the perindopril and indapamide combination as demonstrated in stratified analysis. (Gorelick, 2002) A key message derived from PROGRESS is that greater BP-lowering may be associated with more significant benefit in terms of reducing major vascular events. In MOSES, 1405 patients from general-type medicine clinics with a history of cerebrovascular events were randomized in an open-label trial to either the angiotensin receptor blocker, eprosartan, or the calcium channel blocker, nitrendipine. (Schrader *et al.*, 2005) Approximately 75% of the subjects reached the treatment goal of BP 140/90 mm Hg, and by the end of the trial, BPs were nearly the same in the 2 groups. Although not the primary end point, fatal and nonfatal cerebrovascular events were statistically significantly reduced favoring the eprosartan treatment group, as was the primary end point, combined cerebrovascular and cardiovascular events and noncardiovascular death. The interpretation of these results have been questioned because of the inclusion of transient ischemic attacks (which may not be as clinically relevant as completed strokes) in the primary composite end point and secondary end points for all cerebrovascular events.

In PRoFESS, 20 332 patients with ischemic stroke were randomized to either the angiotensin receptor blocker, 80 mg/day telmisartan (n10 146), or placebo (n10 186) on a background of standard antihypertensive therapy as part of a 22 factorial design study, which also included aspirin plus extended-release dipyridamole plus versus clopidogrel. During the average follow-up period of 2.5 years, mean BP was 3.8/2.0 mm Hg lower in the telmisartan treatment, although at 1 month and 1 year, the between-group difference in SBP was 5.4 and 4.0 mm Hg, respectively, showing that the BP difference favoring telmisartan had narrowed over time. There

was no significant interaction between the BP-lowering or antiplatelet arms of the study. Overall, there were fewer recurrent stroke events in the telmisartan treatment group compared with the placebo group (8.7% versus 9.2%; hazard ratio 0.95; 95% CI, 0.87 to 1.01), but this did not reach statistical significance ($P=0.23$). (Yusuf *et al.*, 2008) Major cardiovascular events were less frequent in the telmisartan group (13.5% versus 14.4%; hazard ratio 0.94; 95% CI, 0.87 to 1.01), but this was not a statistically significant difference ($P=0.11$). Of note, hypotensive symptoms (3.9% versus 1.8%; $P=0.001$) and syncope (0.2% versus 0.1%; $P=0.004$) led to discontinuation of study medication more frequently in the telmisartan group as did diarrhea (0.7% versus 0.4%; $P=0.02$) and nausea (1.0% versus 0.7%; $P=0.01$). Post hoc exploratory analysis suggested that the effect of telmisartan might be time-dependent because there was no significant difference in event rates in the first 6 months after randomization for the primary outcome (a modest increase in events was noted) with a difference favoring telmisartan emerging later. Had the trial been carried out for a longer period of time, it has been speculated that a significant benefit of telmisartan may have been noted. Finally, a nonsignificant trend for a lower rate of new-onset diabetes mellitus was associated with telmisartan treatment (1.2% versus 1.5%; $P=0.10$).

Table 3. AHA/ASA Recommendations for BP Management for Prevention of Recurrent Stroke (Sacco *et al.*, 2006)

1. Antihypertensive treatment is indicated to prevent recurrent stroke and other vascular events; for ischemic stroke, treatment is initiated beyond the hyperacute stroke period.
2. The absolute target BP level is uncertain and should be individualized by patient; benefit may be noted with an average BP drop of 10/5 mm Hg.
3. Lifestyle modifications are included as part of a comprehensive approach.
4. Choice of antihypertensive drug(s) remains uncertain; a diuretic or diuretic plus an angiotensin-converting enzyme inhibitor is a reasonable choice; however, compelling indications may exist for a specific class of antihypertensive and use of the JNC 7 report is recommended.

Questions and Answers about BP Management for Recurrent Stroke Prevention

When Is It Safe to Lower BP After an Acute Ischemic Stroke for the Purpose of Recurrent Stroke Prevention? Answer: While awaiting the arrival of more definitive data, the available evidence suggests that it might be reasonable to start oral antihypertensives as soon as 24 to 72 hours after onset of symptoms provided there are no contraindications such as a presumed hemodynamic mechanism of stroke. (Schrader *et al.*, 2003; Lewin, 2008) The AHA/ASA guideline supports BP-lowering therapy as soon as 24 hours after acute ischemic stroke. (Adams *et al.*, 2007)

What Is the Target BP Goal?

Answer: The precise target goal is not definitively known. In the PROGRESS trial, BP was lowered by approximately 10 / 5 mm Hg, and this BP target has been suggested as a reasonable one for patients according to the AHA/ASA guideline. (Sacco *et al.*, 2006) However, there is variability of absolute BP level

and response to BP-lowering by the patient, especially when age is taken into account, and this must be considered before attempting to lower BP. A reasonable goal, if it can be safely achieved after ischemic stroke, is the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) target of 140 / 90 mm Hg for uncomplicated hypertensive patients and 130/80 mm Hg for those with diabetes mellitus or chronic kidney disease. (Chobanian *et al.*, 2003) Persons without hypertension may also benefit from BP-lowering in relation to recurrent stroke prevention. (Sacco *et al.*, 2006)

Which BP-Lowering Agent Is Most Effective? Answer: In general, all major classes of BP-lowering agents may diminish recurrent stroke risk. Although some studies have suggested that angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be more effective in recurrent stroke prevention than other antihypertensive agents, this assertion has not been validated in more recent studies. Thus far and based on somewhat limited data, the degree of BP-lowering may be more important than the agent used. The choice of the antihypertensive agent should probably depend more on the associated medical conditions rather than any specific cerebrovascular protective effects of a specific class of antihypertensive agents. β -blockers may have a reduced ability to protect against stroke (particularly atenolol), may favor weight gain, and cause dyslipidemia and impaired glycemic control. Therefore, persons at risk for or with multiple metabolic factors may not be good candidates for β -blocker administration unless they are vasodilator β -blockers, which may not be associated with these latter side effects. Thiazide diuretics also may have dyslipidemic and diabetogenic effects when used at high doses, although this has been questioned by the findings of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack trial that failed to support the preference for calcium channel blockers, β -blockers, or angiotensin-converting enzyme inhibitors compared with thiazide-type diuretics in patients with metabolic syndrome. (Wright *et al.*, 2008) The AHA/ASA guideline recommends consideration of a diuretic in combination with an angiotensin-converting enzyme inhibitor. (Sacco *et al.*, 2006)

Guidelines

Table 3 lists recommendations for BP management according to AHA/ASA guidelines. (Sacco *et al.*, 2006) Select recent guides from other regions are referenced. (European Stroke Organisation (ESO), 2008; Kjellstrom *et al.*, 2006) The JNC 7 is an excellent guide for overall BP management. (Chobanian *et al.*, 2003)

Conclusion

The management of hypertension in the setting of an acute stroke is a vexing clinical problem. Recent data suggest that lowering BP in acute ICH is probably safe; however, it remains to be seen if this decreases hematoma expansion or improves outcome. Blood pressure management in acute ischemic stroke remains problematic and questions such as when to start antihypertensives and by how much to reduce BP are yet to be resolved. Although lowering BP is effective for recurrent stroke prevention, the degree of BP reduction may be more important than the class of the agent used.

REFERENCES

- Adams HP Jr, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, Grubb RL, Higashida RT, Jauch EC, Kidwell C, Lyden PD, Morgenstern LB, Qureshi AI, Rosenwasser RH, Scott PA, Wijidicks EF; American Heart Association, American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the Am Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke*. 2007;38: 1655–1711.
- Anderson CS, Huang Y, Wang JG, Arima H, Neal B, Peng B, Heeley E, Skulina C, Parsons MW, Kim JS, Tao QL, Li YC, Jiang JD, Tai LW, Zhang JL, Xu E, Cheng Y, Heritier S, Morgenstern LB, Chalmers J, INTERACT Investigators. Intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT): a randomised pilot trial. *Lancet Neurol*. 2008;7:391–399.
- Bath P, Chalmers J, Powers W, Beilin L, Davis S, Lenfant C, Mancia G, Neal B, Whitworth J, Zanchetti A; International Society of Hypertension Writing Group. International Society of Hypertension (ISH): statement on.
- Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ; HYVET Study Group. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med*. 2008;358:1887–1898.
- Blood pressure in Acute Stroke Collaboration (BASC). Interventions for deliberately altering blood pressure in acute stroke. *Cochrane Database Syst Rev*. 2001;3:CD000039.
- Boulanger JM, Hill MD, CHEP (Canadian Hypertension Educational Program). Hypertension and stroke: 2005 Canadian Hypertension Educational Program recommendations. *Can J Neurol Sci*. 2005;32:403–408.
- Britton M, Carlsson A, de Faire U. Blood pressure course in patients with acute stroke and matched controls. *Stroke*. 1986;17:861–864.
- Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, Mayberg M, Morgenstern L, Ogilvy CS, Vespa P, Zuccarello M. American Heart Association, American Stroke Association Stroke Council, High Blood Pressure Research Council, Quality of Care and Outcomes in Research Interdisciplinary Working Group. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: a guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group. *Stroke*. 2007;38:2001–2023.
- Brott T, Broderick J, Kothari R, Barsan W, Tomsick T, Sauerbeck L, Spilker J, Duldner J, Khoury J. Early hemorrhage growth in patients with intracerebral hemorrhage. *Stroke*. 1997;28:1–5.

- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ. National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289:2560–2572.
- Davis SM, Broderick J, Hennerici M, Brun NC, Diringer MN, Mayer SA, Begtrup K, Steiner T; Recombinant Activated Factor VII Intracerebral Hemorrhage Trial Investigators. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. *Neurology*. 2006;66:1175–1181.
- Elliott WJ. Systemic hypertension. *CurrProblCardiol*. 2007;32: 201–259.
- European Stroke Initiative Writing Committee, Writing Committee for the EUSI Executive Committee, Steiner T, Kaste M, Forsting M, Mendelow D, Kwicinski H, Szikora I, Juvela S, Marchel A, Chapot R, Cognard C, Unterberg A, Hacke W. Recommendations for the management of intracranial haemorrhage—part I: spontaneous intracerebralhaemorrhage. The European Stroke Initiative Writing Committee and the Writing Committee for the EUSI Executive Committee. *Cerebrovasc Dis*. 2006;22:294–316.
- European Stroke Organisation (ESO) Executive Committee, ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovasc Dis*. 2008;25:457–507.
- Fischberg GM, Lozano E, Rajamani K, Ameriso S, Fisher MJ. Stroke precipitated by moderate blood pressure reduction. *J Emerg Med*. 2000; 19:339–346.
- Fogelholm R, Avikainen S, Murros K. Prognostic value and determinants of first-day mean arterial pressure in spontaneous supratentorial intracerebral hemorrhage. *Stroke*. 1997;28:1396–1400.
- Gorelick PB. New horizons for stroke prevention: PROGRESS and HOPE. *Lancet Neurol*. 2002;1:149–156.
- Hays A, Diringer MN. Elevated troponin levels are associated with higher mortality following intracerebral hemorrhage. *Neurology*. 2006;66: 1330–1334.
- Jauch EC, Lindsell CJ, Adeoye O, Khoury J, Barsan W, Broderick J, Pancioli A, Brott T. Lack of evidence for an association between hemodynamic variables and hematoma growth in spontaneous intracerebral hemorrhage. *Stroke*. 2006;37:2061–2065.
- Kjellstrom T, Norrving B, Shatchkute A. Helsingborg Declaration 2006 on European stroke strategies. *Cerebrovasc Dis*. 2007;23:231–241.
- Kuwata N, Kuroda K, Funayama M, Sato N, Kubo N, Ogawa A. Dysautoregulation in patients with hypertensive intracerebral hemorrhage. A SPECT study. *Neurosurg Rev*. 1995;18:237–245.
- Lawes CM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: an overview of published reviews. *Stroke*. 2004;35:1024.
- Leonardi-Bee J, Bath PM, Phillips SJ, Sandercock PA; IST Collaborative Group. Blood pressure and clinical outcomes in the International Stroke Trial. *Stroke*. 2002;33:1315–1320.
- Lewin S. Continue or stop post-stroke antihypertensives study (COSSACS). Principal Investigators: Professor TG Robinson, Professor JF Potter. 2008. Available at: www.le.ac.uk/cv/research/COSSACS/COSSACHome.htm l. Accessed July 4, 2008.
- Ohwaki K, Yano E, Nagashima H, Hirata M, Nakagomi T, Tamura A. Blood pressure management in acute intracerebral hemorrhage: relationship between elevated blood pressure and hematoma enlargement. *Stroke*. 2004;35:1364–1367.
- Okumura K, Ohya Y, Maehara A, Wakugami K, Iseki K, Takishita S. Effects of blood pressure levels on case fatality after acute stroke. *J Hypertens*. 2005;23:1217–1223.
- Pedely L, Gorelick PB. Chronic management of blood pressure after stroke. *Hypertension*. 2004;44:1–5.
- Potter JF, Robinson TG, Ford GA, Mistri A, James M, Chernova J, Jagger C. Controlling hypertension and hypotension immediately poststroke (CHHIPS): a randomised, placebo-controlled, double-blind pilot trial. *Lancet Neurol*. 2009;8:48–56.
- Powers WJ, Zazulia AR, Videen TO, Adams RE, Yundt KD, Aiyagari V, Grubb RL Jr, Diringer MN. Autoregulation of cerebral blood flow surrounding acute (6 to 22 hours) intracerebral hemorrhage. *Neurology*. 2001;57:18–24.
- PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet*. 2001;358:1033–1041.
- Qureshi AI. Acute blood pressure management—the North American perspective. Update on cerebral hemorrhage trials session. Presented at the International Stroke Conference; New Orleans; February 20, 2008. Available at: www.scienceondemand.org/stroke2008/sessions/player.html?sid08020172.758. Accessed July 4, 2008.
- Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. American Heart Association, American Stroke Association Council on Stroke, Council on Cardiovascular Radiology and Intervention, American Academy of Neurology. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke*. 2006;37:577–617.
- Schrader J, Luders S, Kulschewski A, Berger J, Zidek W, Treib J, Einhaupl K, Diener HC, Dominiak P; Acute Candesartan Cilexetil Therapy in Stroke Survivors Study Group. The ACCESS Study: evaluation of Acute Candesartan Cilexetil Therapy in Stroke Survivors. *Stroke*. 2003;34:1699–1703.
- Schrader J, Luders S, Kulschewski A, Hammersen F, Plate K, Berger J, Zidek W, Dominiak P, Diener HC; MOSES Study Group. Morbidity and Mortality After Stroke, Eprosartan Compared with Nitrendipine for Secondary Prevention: principal results of a prospective randomized controlled study (MOSES). *Stroke*. 2005;36:1218–1226.
- the management of blood pressure in acute stroke. *J Hypertens*. 2003;21: 665–672.
- Wityk RJ. Blood pressure augmentation in acute ischemic stroke. *J Neurol Sci*. 2007;261:63–73.
- Wright JT Jr, Harris-Haywood S, Pressel S, Barzilay J, Baimbridge C, Bareis CJ, Basile JN, Black HR, Dart R, Gupta AK, Hamilton BP, Einhorn PT, Haywood LJ, Jafri

- SZ, Louis GT, Whelton PK, Scott CL, Simmons DL, Stanford C, Davis BR. Clinical outcomes by race in hypertensive patients with and without the metabolic syndrome: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Arch Intern Med.* 2008;168:207–217.
- Yusuf S, Diener HC, Sacco RL, Cotton D, Ounpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlof B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, Pais P, Roberts R, Skvortsova V, Teal P, Toni D, VanderMaelen C, Voigt T, Weber M, Yoon BW; PROFESS Study Group. Telmisartan to prevent recurrent stroke and cardiovascular events. *N Engl J Med.* 2008;359: 1225–1237.
- Zazulia AR, Diringner MN, Videen TO, Adams RE, Yundt K, Aiyagari V, Grubb RL Jr, Powers WJ. Hypoperfusion without ischemia surrounding acute intracerebral hemorrhage. *J Cereb Blood Flow Metab.* 2001;21: 804–810.
