Management of Blood Pressure in Patients with Cerebrovascular Disease

Jacob S. Elkins, MD

ABSTRACT

PURPOSE: To review guidelines and trial data pertinent to blood pressure management in patients with cerebrovascular disease.

EPIDEMIOLOGY: Hypertension is the largest contributor to the overall societal burden of stroke. For example, it is estimated that approximately 40% of first-time strokes among individuals in their 50s and 60s are attributable to hypertension.1 Although the methods and benefits of treating hypertension in the general population are widely known, there has been greater uncertainty historically about the treatment of blood pressure in those with established cerebrovascular disease.

REVIEW SUMMARY: Treating hypertension substantially reduces the risk of recurrent stroke. Evidence from several large trials involving patients with stroke or cardiovascular disease indicates that clinicians should consider pharmacologic lowering of blood pressure after stroke even when blood pressure does not meet diagnostic criteria for hypertension. Although there are persistent concerns about the effect of lowering blood pressure on cerebral perfusion in the acute stroke setting, available empirical data do not support higher blood pressure targets in the chronic phases of cerebrovascular disease.

TYPE OF AVAILABLE EVIDENCE: Nationally recognized treatment guidelines, randomized controlled studies.

GRADE OF AVAILABLE EVIDENCE: Good to fair. Some trial data may not be fully generalizable to stroke patients because only a minority of included subjects had a history of stroke.

CONCLUSION: Reducing blood pressure prevents recurrent stroke in patients with cerebrovascular disease. Although individualization of therapy is needed, long-term benefits of antihypertensive therapy appear broadly applicable to stroke patients regardless of stroke mechanism or history of hypertension.


EPIDEMIOLOGY

Hypertension is the largest contributor to the overall societal burden of stroke. For example, it is estimated that approximately 40% of first-time strokes among individuals in their 50s and 60s are attributable to hypertension.1 Although the methods and benefits of treating hypertension in the general population are widely known, there has been greater uncertainty historically about the treatment of blood pressure in those with established cerebrovascular disease.

In several different community-based studies of stroke survivors, approximately 20% to 30% of individuals with measured blood pressures greater than 140/90 mm Hg were not receiving pharmacologic blood pressure therapy during the first year after stroke.2-4 Of those patients receiving medications, only 40% actually achieved blood pressures below 140/90 mm Hg.5 Such numbers are moderately worse than the also low rates of hypertension treatment after myocardial infarction.6 There are several unique

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aspects of the relationship between blood pressure and cerebrovascular disease that may play a role in influencing physician decision making about antihypertensive therapy, particularly physiologic concerns about lowering blood pressure in those patients with stenoses of the craniovascular vessels or impaired cerebral autoregulation. In this review, we will focus on the unique aspects of blood pressure control in patients with cerebrovascular disease and review the empiric data that help to guide treatment decisions.

**Clinical Scenario**

A 70-year-old woman had an occipital lobe stroke 3 months ago. A series of tests revealed that this stroke was most likely due to vertebral artery stenosis. Currently the patient is asymptomatic. She is taking aspirin and atorvastatin. During a routine physical examination her blood pressure is measured at 132/85 mm Hg. What blood pressure treatment is most effective for reducing the risk of recurrent stroke?

**Treatment Options: Lifestyle Modification and Pharmacologic Therapy**

After secondary causes of hypertension have been considered and excluded, there are 2 main options for treating blood pressure: lifestyle modification and pharmacologic therapy. Treatment guidelines generally recommend lifestyle modification (weight loss, reduction of sodium intake, avoidance of excess alcohol consumption, daily exercise, and use of the Dietary Approaches to Stop Hypertension eating plan) when the measured systolic blood pressure is greater than 120 mm Hg or a diastolic blood pressure is greater than 80 mm Hg (Table). Lifestyle modification reduces blood pressure without the risks and expense of medications, enhances the efficacy of pharmacotherapy, and improves control of multiple cardiovascular risk factors. However, the ability of lifestyle modification to specifically reduce cardiovascular event rates remains largely untested. Therefore, a major question that confronts clinicians is when pharmacologic therapy is needed in addition to lifestyle changes. Although there is general agreement about the need for pharmacologic therapy in patients who meet standard criteria for hypertension, there is considerably more debate about drug treatment when the blood pressure does not meet these criteria. According to the widely referenced JNC-7 guidelines (Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) and the Veterans Administration/Department of Defense guidelines, the patient just described falls into a JNC-7 category of "prehypertension" for which lifestyle modification is the mainstay of recommended therapy. Although the JNC-7 guidelines make an explicit mention of the need for pharmacologic blood pressure treatment in patients with diabetes and in those with chronic kidney disease when blood pressure is in the prehypertension range, a similar exception is not made for patients with cerebrovascular disease. In contrast, the recent 2006 American Heart Association guidelines for secondary stroke prevention state that blood pressure therapy "should be considered" for all stroke and transient ischemic attack (TIA) patients, regardless of hypertension status (Table). The results from 2 large trials have strongly influenced the way that stroke specialists now think about antihypertensive therapy for secondary stroke prevention. The Heart Outcomes Prevention Evaluation (HOPE) study compared the effects of the angiotensin-converting enzyme (ACE) inhibitor, ramipril, with placebo in 9297 high-risk patients with vascular disease or diabetes plus one other cardiovascular risk factor. The mean blood pressure in all subjects at entry was 139/79 mm Hg. Therapy with ramipril

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**Table. Hypertension Guidelines for Patients with Cerebrovascular Disease**

<table>
<thead>
<tr>
<th>JNC-VII</th>
<th>VA/DoD</th>
<th>AHA/ASA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehypertension</td>
<td>Lifestyle modification</td>
<td>Lifestyle modification</td>
</tr>
<tr>
<td>Hypertension</td>
<td>ACE-I and thiazide</td>
<td>ACE-I and thiazide</td>
</tr>
<tr>
<td>Treatment goal</td>
<td>&lt;140/90 mm Hg</td>
<td>&lt;140/90 mm Hg</td>
</tr>
<tr>
<td>Timing of therapy</td>
<td>Control BP at intermediate levels (~160/100 mm Hg) until condition is stabilized or improved</td>
<td>Not described</td>
</tr>
</tbody>
</table>

ACE-I = angiotensin-converting enzyme inhibitor; AHA/ASA = American Heart Association/American Stroke Association; BP = blood pressure; DoD = Department of Defense; JNC-VII = The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; VA = Veterans Administration. Data from Chobanian et al; Veterans Administration, Department of Defense; Sacco et al.
resulted in a 32% relative risk reduction (RRR) for stroke when compared to placebo (95% confidence interval [CI], 45%–26%; P < .001). Importantly, the benefits of ramipril therapy appeared to be similar when individuals with baseline systolic blood pressure (SBP) 129 mm Hg or lower were compared to those with baseline SBP 140 mm Hg or higher (P for heterogeneity = .89). Although the benefits of ramipril for stroke prevention also appeared similar in those patients with and without a history of stroke (P for heterogeneity = .21), only approximately 10% of subjects in the HOPE trial had a history of stroke, thus confirmation of the benefit in stroke patients, especially in those without hypertension, was needed. This confirmation came in the Perindopril Protection Against Recurrent Stroke Study (PROGRESS) in which 6105 patients with prior ischemic or hemorrhagic stroke were randomized to an ACE inhibitor, perindopril, with or without the diuretic indapamide, or placebo. Again, RRR for stroke were nearly identical in those patients with and without hypertension at study entry (RRR 32% vs 34%). Although the PROGRESS trial analysis defined hypertension as SBP 160 mm Hg or higher or diastolic blood pressure (DBP) 90 mm Hg or higher, approximately 75% of the subjects classified as nonhypertensive would have met the standard definition of SBP 140 mm Hg or lower and DBP 90 mm Hg or lower. A recent systematic review has also confirmed the finding that the benefits of pharmacologic blood pressure therapy in stroke patients is similar in patients with and without a history of hypertension. Therefore, although it is important to be cautious about generalizing trial results to all subjects eligible for trial inclusion, the available data support the hypothesis that pharmacologic treatment of blood pressure will prevent recurrent stroke even when the blood pressure is below the standard cut-points used to define hypertension.

**GOALS OF THERAPY**

Even if one agrees that pharmacologic blood pressure treatment is indicated in this patient scenario, there is generally less consensus about the actual goals of therapy. For example, whether physicians should attempt to achieve a specific target blood pressure, a specific absolute reduction in blood pressure, or withhold pharmacologic treatment when blood pressure is below a certain level remain areas of debate. The results of the PROGRESS and HOPE trials provide somewhat conflicting results about the need to achieve absolute reductions in blood pressure. In the HOPE trial, the benefits of therapy with ramipril for stroke and for combined cardiovascular events were robust even though there were only small differences in the measured blood pressures between the active and placebo groups at the end of the study (136/76 vs 139/77). In contrast, in the PROGRESS trial, which only included stroke and TIA patients, there was minimal benefit of monotherapy with an ACE inhibitor for stroke prevention compared to placebo (RRR 5%), whereas there was a dramatic benefit with the combination of an ACE inhibitor and a thiazide diuretic (RRR 43%; P for difference in effect between treatment groups <.001). One common explanation for this difference in efficacy was the greater absolute reduction in blood pressure in the ACE/thiazide combination group compared to the ACE-only group (12.3/5 mm Hg vs 4.9/2.8 mm Hg). A recent meta-analysis of more than 40 randomized controlled trials supported the findings of the PROGRESS study, showing that a 10-mm Hg reduction in systolic BP was associated with a decrease in stroke risk of approximately 33% and that the benefits of this lowering were similar in patients with differing baseline blood pressures or cardiovascular histories (Figure). Furthermore, a sub-study of the HOPE trial that used ambulatory blood pressure monitoring found more substantial effects of ramipril on 24-hour average blood pressure than on office measurements of blood pressure, suggesting that the blood pressure effects of ramipril may have been more important to the stroke risk reduction than originally considered. Therefore, most data support the idea that the benefits of blood pressure therapy are related to the actual reductions in blood pressure that they achieve and, if response is poor, additional agents or dose escalation should be considered.

![Figure. The Benefits of Blood Pressure Reduction (Versus Placebo or No Treatment) by Subgroup: A Meta-Analysis of More Than 40 Randomized Trials](image-url)

<table>
<thead>
<tr>
<th>Blood pressure lowering trials</th>
<th>Net difference in SBP/DBP</th>
<th>Relative risk reduction of stroke (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 years</td>
<td>12/4</td>
<td>40% (26%–52%)</td>
</tr>
<tr>
<td>60–69 years</td>
<td>6/3</td>
<td>28% (23%–35%)</td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>13/6</td>
<td>28% (21%–35%)</td>
</tr>
<tr>
<td>Mean baseline SBP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;140 mm Hg</td>
<td>3/1</td>
<td>30% (15%–42%)</td>
</tr>
<tr>
<td>140–160 mm Hg</td>
<td>10/4</td>
<td>26% (17%–34%)</td>
</tr>
<tr>
<td>&gt;160 mm Hg</td>
<td>13/6</td>
<td>32% (25%–38%)</td>
</tr>
<tr>
<td>History of stroke/TIA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Few/no participants</td>
<td>11/5</td>
<td>35% (28%–41%)</td>
</tr>
<tr>
<td>Most/all participants</td>
<td>9/4</td>
<td>22% (12%–31%)</td>
</tr>
<tr>
<td>History of vascular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Few/no participants</td>
<td>13/6</td>
<td>38% (30%–45%)</td>
</tr>
<tr>
<td>Most/all participants</td>
<td>6/3</td>
<td>24% (16%–31%)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>30% (26%–32%)</td>
</tr>
</tbody>
</table>

CI = confidence interval; DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischemic attack. Reprinted with permission from Lawes et al. Stroke. 2004;35:776-785.
Estimates from large cohort studies show a linear increase in stroke risk beginning at about 120/80 mm Hg. Therefore, it would seem reasonable that there is less benefit to be gained from additional blood pressure reduction when the blood pressure is below 120/80 mm Hg. However, whether such a cut-off point is applicable to high-risk stroke patients is not certain, and randomized trials of stroke patients have not reported a plateau effect of blood pressure therapy among those who are normotensive (SBP <120 mm Hg and DBP <80 mm Hg) at the time of enrollment. Furthermore, there is reason to have some skepticism about withholding treatment based on casual, office measurements of blood pressure. Blood pressure is an inherently variable measurement and physicians generally have less information about a patient’s true average blood pressure or circadian variations in blood pressure when compared, for example, to the blood sugar logs recorded by patients with diabetes. There is growing interest in the phenomenon of “masked hypertension,” which occurs when individuals meet definitions of hypertension on ambulatory monitoring but not when blood pressure is measured in the office. The true prevalence of masked hypertension is unknown, but current estimates suggest that it is as high as 10% in the general population. Several studies have found that the risks associated with masked hypertension are very similar in magnitude to the risks associated with traditional hypertension. Therefore, although there is likely to be a lower limit at which further reductions in blood pressure are not helpful, this limit has not been adequately defined and it is often difficult for physicians to know an individual’s true blood pressure exposure. Consequently, especially in high-risk individuals who experience no adverse effects, lowering blood pressure even when it is in the normal range during office visits could provide extra protection against recurrent stroke.

CHOICE OF AGENTS

There is growing interest in the theory that some classes of blood pressure therapy provide protective effects against stroke that are independent of their blood pressure-lowering effects. Several recent studies have provided guidance on this issue with head-to-head comparisons of various ACE inhibitors, beta-blockers, calcium channel blockers (CCBs), and angiotensin receptor blockers (ARBs) in high-risk patients or those with established vascular disease:

• In the Losartan Intervention For Endpoint Reduction in Hypertension study (LIFE), a group of 1195 patients with diabetes, hypertension (mean 177/96 mm Hg), and signs of left ventricular hypertrophy were randomized to the ARB losartan or the beta-blocker atenolol. Despite identical reductions in blood pressure over the 4 years of monitoring, the cardiovascular morbidity and mortality were lower in the ARB group (relative risk 0.76; 95% CI 0.58–0.98; P = .31), as was the all-cause mortality (relative risk 0.61; 95% CI 0.45–0.84; P = .002). These differences in cardiovascular mortality were driven by a 25% reduction in stroke risk in the losartan group compared to the atenolol group (P <.001). Meta-analyses have also found that beta-blockers appear to be less effective than other agents for stroke prevention.

• In the Morbidity and Mortality After Stroke, Eprosartan Compared with Nitrendipine for Secondary Prevention (MOSES) study, 1405 hypertensive patients with a stroke during the past 24 months were randomized to the ARB or the long-acting CCB nitrendipine and followed for a mean of 2.5 years. As in the LIFE study, the beginning and ending mean ambulatory blood pressures were similar in the 2 treatment groups: changing from 151/84 mm Hg to 138/81 mm Hg in the eprosartan group, and from 152/87 mm Hg to 136/80 mm Hg in the nitrendipine group. Despite these comparable blood pressure reductions, there were fewer strokes in the ARB group (102) than in the CCB group (134; relative risk 0.75; 95% CI 0.58–0.97; P = .03).

• It is still uncertain whether angiotensin receptor blockade differs in efficacy for stroke prevention when compared to ACE inhibition. Some comparison trials in subjects with cardiovascular disease have been performed. The Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan compared the effects of an ACE inhibitor (captopril) against those of an ARB (losartan) in 5477 patients with complicated acute myocardial infarctions. In this setting, the rates of all-cause deaths in the captopril group (16%) and losartan group (18%) were not significantly different (relative risk 1.13 favoring captopril; 95% CI 0.99–1.28; P = .07).

• Despite the potential benefits of blood pressure modulation with ACE inhibitors or ARBs in preventing stroke, thiazide diuretics remain a reasonable alternative as first-line therapy, particularly for African Americans. For example, in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, chlorthalidone was equivalent to lisinopril for blood pressure reduction and primary stroke prevention in white patients and superior among African American patients; further, the risk of ACE inhibitor-associated angioedema was 2 to 4 times higher in African American patients compared to white patients.

• Although head-to-head trials of blood pressure medications are often used to make inferences
about entire classes of antihypertensive medications, it is generally not possible to know whether results from these trials can be extrapolated to all members of a particular class. For example, ramipril may be more effective than other ACE inhibitors for stroke prevention and chlorthalidone may have advantages over the more commonly used diuretic, hydrochlorothiazide. Given that many agents used in trials are still protected by patents, the willingness of physicians to substitute a less costly member of a particular drug class could have large implications for healthcare costs.

When considering differential effects in drug efficacy, it is worth noting that most of the benefit of a blood pressure medication appears to be mediated by its actual effect on blood pressure. Therefore, although an ARB may be more effective than a beta-blocker in preventing stroke for the same reduction in blood pressure, beta-blockers could be superior if an individual's blood pressure responds better to the beta-blocker than the ARB. Although available studies suggest that initiating therapy with ACE, ARB, and/or thiazides may be preferable for stroke patients, current guidelines continue to emphasize the importance of blood pressure control over the actual agents used.11

**SAFETY OF BLOOD PRESSURE THERAPY AFTER STROKE**

The clinical scenario states that the patient's stroke occurred 3 months ago. The issue of when to initiate blood pressure therapy after stroke is an important one. Current guidelines for the treatment of acute ischemic stroke recommend not treating hypertension in the acute setting unless the SBP is greater than 220 mm Hg or the DBP is greater than 120 mm Hg (excluding thrombolytic patients and those with signs of active end-organ injury, such as aortic dissection).38 Although this recommendation is not based on firm empiric evidence and remains an area of debate, it is currently followed by many stroke neurologists. From a physiologic perspective, there are arguments to be made for and against lowering blood pressure in the acute stroke setting. For example, lowering blood pressure may reduce edema formation and lower the chance of hemorrhagic conversion of the infarction.39,40 However, the primary concern with lowering blood pressure in acute stroke is related to its potential effects on perfusion of the penumbral tissue around the area of core infarction.39 Ischemia appears to impair the homeostatic mechanisms that mediate cerebral autoregulation.41 Blood flow studies in stroke patients have documented cases in which blood flow in ischemic brain is proportional to systemic blood pressure, as opposed to in the normal brain in which autoregulation maintains flow at a constant rate over a wide range of systemic blood pressures.41,42 The possibility of so-called “pressure-passive” flow has led some to hypothesize that pharmacologic elevation of blood pressure may help to preserve tissue at risk in acute stroke.39,41

It is uncertain how long the impairment of autoregulation may persist after stroke, but it may be as long as several months, and several anecdotal reports have documented the recrudescence of stroke symptoms after blood pressure falls below a certain critical threshold in the subacute stroke period.39,42

Currently, available studies provide little guidance on when it is safe to restart blood pressure medications after stroke. In one medium-size trial involving 342 hypertensive patients with acute ischemic stroke, subjects were randomized to an ARB or placebo for the first 7 days after stroke (and then all subjects received the active treatment).37 Although there were no concerns about safety identified in this trial and the ARB arm had improvement in long-term cardiovascular endpoints, it is important to note that the recorded blood pressures were essentially identical between the 2 groups throughout the study period. The median time from stroke to initiation of blood pressure therapy was 8 months in the PROGRESS trial and 12 months in the MOSES trial, the 2 largest studies of a blood pressure intervention in stroke patients. In the MOSES trial, less than 3% of subjects were enrolled in the first week after stroke. However, in practice, concerns over impaired cerebral autoregulation need to be balanced against the problem of undertreatment of hypertension in stroke patients and the well-documented long-term benefits of blood pressure therapy. Some centers have instituted standard protocols for initiating blood pressure therapy at the time of hospital discharge to improve adherence to therapy and limit the possibility that appropriate blood pressure medications will never be initiated.38 In the PROGRESS trial, investigators chose a 2-week minimum time from stroke before subjects could be randomized to blood pressure therapy. Current guidelines endorse starting blood pressure therapy as soon as a subject is out of the “hypercute” stroke period.11

Safety issues are also an important concern when considering the use of the more aggressive blood pressure targets that may benefit stroke patients. Although concerns about loss of autoregulation are most prominent in acute ischemia, lowering blood pressure also poses theoretic risks of brain injury due to hypoperfusion in the chronic phase after stroke.39 White matter disease is common among hypertensives in which it is associated with arteriosclerosis, loss of dilatory capacity in resistance vessels, and orthostasis.40,41 White matter lesions are thought to be heterogeneous in etiology, but many demonstrate pathologic and biochemical features of ischemia,42 leading some to speculate that pharmacologic lowering of blood pressure could further aggravate this injury.39 If true, it is possible that lowering blood pressure could, in some instances, worsen cognitive function and mobility, which are established clinical correlates of white matter
injury. Additional studies will be needed to define whether there are some individuals in which risks due to hypoperfusion from blood pressure therapy outweigh its proven benefits in terms of preventing progression of underlying cerebrovascular disease. In the meantime, it seems prudent to consider lower initial drug doses, avoiding rapid dose titrations, and making more frequent safety checks when treating hypertension in those patients with cerebrovascular disease, particularly when they are elderly, taking multiple medications, or have a high burden of whiter matter injury.

**Blood Pressure Therapy and Stroke Subtype**

The final aspect of this clinical scenario that warrants discussion is the presence of vertebral artery stenosis. In general, proper stroke prevention is dictated by identifying, as best as possible, the cause of the stroke. However, in the case of blood pressure therapy, it is less clear whether and how physicians should incorporate information about stroke cause into their decision making. The existence of a stenosis in the cranio-cervical circulation, particularly when high-grade, is typically a major source of concern when it comes to starting blood pressure medications. If such patients are at the limit of their autoregulatory capacity (ie, their cerebral resistance vessels are maximally dilated in order to maintain cerebral perfusion distal to the stenosis), lowering blood pressure could in theory cause a stroke to occur. These patients are frequently excluded from trials of protocols that involve lowering blood pressure after stroke, a practice that creates further uncertainty about when such therapy may be safe for them. When such a stenosis is located in the cervical carotid artery and endarterectomy is planned, blood pressure therapy is often delayed until the procedure is performed. However, when stenoses occur at other locations in the cerebrovascular, the role of endovascular or surgical correction is less established and less commonly performed. Although such patients may be at risk for adverse effects on cerebral perfusion when blood pressure is lowered, they are a very high-risk group of patients for stroke recurrence in general. Because blood pressure therapy is a major way to reduce stroke risk, a trial of gradual blood pressure lowering is often indicated for these patients. Certainly, no major stroke prevention trial using a blood pressure medication has made a specific effort to exclude these subjects from randomization on the basis of safety concerns. In the largest study to date of patients with symptomatic intracranial atherosclerosis confirmed by catheter angiography, there were no data to support the concern that the use of blood pressure medications increased the risk for stroke distal to a stenosis.

Although stroke patients with intracranial stenoses are at potential risk of having hypertension inadequately treated due to safety concerns, other types of stroke patients may be at risk for undertreatment because of the belief that athero- or arteriosclerosis may not have been a significant contributor to the stroke. For example, when a patient with atrial fibrillation has a classic cardioembolic stroke, most physicians would know to treat with long-term warfarin therapy, but they may be less concerned about starting blood pressure medications. However, trial data suggest that physicians should be cautious about not treating blood pressure based on assumptions related to stroke etiology. In a secondary analysis of the PROGRESS trial, active therapy achieved a very similar risk reduction in stroke patients with atrial fibrillation when compared to its effect in patients who had stroke from other causes, even when subjects did not have hypertension at study entry.

**Conclusions**

I would recommend lifestyle modification for this patient but also start therapy with an ACE inhibitor or thiazide diuretic. If this therapy was well tolerated and the blood pressure remained in the prehypertension range during follow-up, I would add the other of these agents and continue to gradually escalate doses or add new agents until the systolic blood pressure was below 120/80 mm Hg. The benefits of treating hypertension are especially pronounced for patients with cerebrovascular disease, and risk reductions can be seen even when the blood pressure is within ranges that do not typically merit treatment in healthier individuals. Although there is scientific interest in the class benefits from inhibitors of the angiotensin system and diuretics for the secondary prevention of stroke, the largest clinical gains are apparent from making absolute reductions in blood pressure and achieving normotension. It is important to consider the unique physiology of cerebrovascular disease as it relates to blood pressure, autoregulation, and cerebral perfusion, especially in the acute stroke setting. While there is justification for careful monitoring, gradual dose escalations, and individualization of blood pressure therapy, the benefits of long-term blood pressure lowering appear to be broadly generalizable to patients after stroke. Although further work is needed to address safety concerns in some stroke patients with compromised cerebral autoregulation, physiologic concerns in isolation should rarely if ever be used to withhold the proven long-term benefits of treating hypertension.

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**References**

MANAGEMENT OF BLOOD PRESSURE


