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# Blood pressure reduction in ischemic stroke

## A two-edged sword?

Karen C. Johnston, MD, MSc; and Stephan A. Mayer, MD

There is convincing evidence that controlling hypertension is effective in primary and secondary stroke prevention. It is less clear whether and how to treat blood pressure (BP) in the setting of acute stroke.<sup>1</sup> In this issue of *Neurology*, Oliveira-Filho et al. provide new data on this issue.<sup>2</sup>

Elevated BP after acute ischemic stroke is frequent and multifactorial although spontaneous reductions are known to occur in the first hours.<sup>3</sup> High initial BP has been associated with poor outcome<sup>4,5</sup> and good outcome,<sup>6,7</sup> resulting in controversy about best management. Concerns remain about BP lowering based on the known animal pathophysiology, which suggests that reductions in systemic BP may reduce cerebral perfusion pressure and blood flow to viable ischemic tissue, particularly in the absence of normal autoregulation.<sup>8,9</sup> However, there is a theoretical risk of increased edema, hemorrhage, or further vascular damage if BP is allowed to remain high.<sup>8</sup>

In the absence of solid data from controlled trials, current acute ischemic stroke guidelines suggest that unless systolic BP exceeds an arbitrary cutoff of 220 mm Hg or diastolic exceeds 120 mm Hg, it should be lowered only if there is coexisting hypertensive end-organ damage (hypertensive encephalopathy, aortic dissection, acute renal failure, acute pulmonary edema, or acute myocardial infarction), or in planned thrombolytic therapy.<sup>10</sup>

These guidelines are supported by anecdotal reports of sudden deterioration after overly aggressive BP reduction in the acute setting (particularly sublingual nifedipine and IV nitroprusside)<sup>11</sup> and by adverse effects in a trial of IV nimodipine given within 24 hours of onset in which poor outcome was directly related to the extent of diastolic BP reduction.<sup>12</sup> As a logical extension of these observations, some patients

with acute stroke have improved when treated with pharmacologic BP elevation.<sup>13</sup> Whereas "lower is better" for primary and secondary prevention, there is a growing sentiment that "high is good" in the acute setting.

However, some uncertainty still exists. A post hoc analysis of the National Institute of Neurological Disorders and Stroke tissue plasminogen activator trial suggests that gentle BP reduction to a lower target of 180/105 is well tolerated, although it remains unclear if this confers any benefit.<sup>14</sup> In this study, there was no difference in the rate of early neurologic deterioration or in 3-month functional outcome in hypertensive placebo-treated patients who had their BP lowered compared to those who did not, and their mortality rate was slightly lower. Further complicating the issue, a recent randomized clinical trial demonstrated a delayed reduction in mortality in patients with acute ischemic stroke who received an angiotensin type 1 receptor blocker for acute BP treatment, despite the absence of a significant effect on BP compared to placebo.<sup>15</sup>

In this issue of *Neurology*, Oliveira-Filho et al. look at the relationship between acute BP reduction and 3-month outcome in patients with acute ischemic stroke.<sup>2</sup> Their prospective study evaluated 115 patients within the first 24 hours of ischemic stroke symptom onset and assessed the independent association between BP lowering and poor outcome. After consideration for the effect of potential confounders in a multivariable analysis, only NIH Stroke Scale score and degree of systolic BP reduction remained independent predictors of poor outcome. The authors demonstrated a nearly twofold increased risk of poor outcome for every 10% decrease in systolic BP reduction in the first 24 hours, regardless of whether anti-hypertensive therapy was given.

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This study offers a prospective, systematic evaluation including frequent early BP measurements allowing a greater understanding of the relationship between BP variation and clinical outcome in this population. The results support anecdotal literature and are of interest and importance despite several limitations. Treatment decisions were left to the discretion of a non-study physician, and the majority of patients received antihypertensive therapy. The design of this study does not allow us to determine the relative contributions of spontaneous vs therapeutic BP reduction nor can causality be assumed. Additionally, because this was a small study in which multiple comparisons were made to assess relationships to outcome, the relationships identified as being present, as well as those that were absent, will require validation in an external dataset. Despite these limitations, these data add new information on risk vs benefit of BP lowering in the acute stroke setting.

The urgency of determining the optimal management of BP in patients with acute stroke has increased as data have suggested that acute hypertension is common and harmful effects may result from aggressive BP reduction. Until we have a definitive, well-designed randomized trial, prudence suggests that if BP is to be lowered in the first 24 hours after stroke, it should be lowered carefully and in a monitored setting with an easily titratable, short-acting agent such as labetalol or nicardipine.<sup>11</sup> In anticipation of more definitive data, however, the Oliveira-Filho et al. study supports current guidelines indicating that BP reduction in the acute stroke setting should be avoided if possible.

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