

Blood Pressure in Acute Stroke Still No Answer for Management

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Whether intravenous or endovascular stroke therapy should be withheld in patients with acute ischemic stroke with blood pressure (BP) levels above certain thresholds is one of the major unresolved issues in acute stroke management. The post hoc analysis of data of the MR CLEAN trial (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) published in *Stroke* adds important new information about the risks and benefits of endovascular therapy (EVT) in acute stroke patients with different BP levels at baseline. Mulder et al¹ analyzed BP and the effect of EVT in the MR CLEAN study and showed that the effectiveness of EVT is similar in the entire range of baseline BP of the included patients. Furthermore, BP and EVT did not interact with the occurrence of symptomatic intracerebral hemorrhage (ICH) or other safety parameters. However, there was an independent association between increasing systolic BP (SBP) levels and the risk of symptomatic ICH in the subgroup of patients with SBP > 120 mm Hg, as shown previously.^{2,3} In addition, the authors found a similar J-shaped relationship of admission BP and functional outcome in patients who underwent EVT and their controls who received intravenous thrombolysis (IVT). The information gained from MR CLEAN provides an important message for clinicians treating patients with acute ischemic strokes with proximal vessel occlusion in the anterior circulation: BP, whatever its value is, does not influence the effectiveness of EVT. Therefore, EVT is indicated for treatment of large-vessel occlusions causing stroke irrespective of admission BP. Neither low nor high BP values advise against EVT. However, the number of patients with high (>185/110 mm Hg) and low BP in the study was small; therefore, no valid conclusions can be made on the safety of EVT in these patients.

It is known for decades that BP in patients with acute stroke is elevated and that high and low BP levels are associated with poor functional outcome.^{4,5} Nevertheless, many relevant questions still remain unresolved.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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What Is the Mechanism of Elevated BP in Patients With Acute Stroke?

BP is increased in ≈3 of 4 patients with acute stroke and mostly decreases spontaneously over the next few days.² However, the mechanism of the transient rise in BP is unknown and the BP increase after major stroke is often claimed to be a stroke-specific response (ie, post-stroke hypertension). We have shown in a population-based study that acute post-stroke BP in patients with ICH was markedly raised when compared with premorbid levels and fell rapidly thereafter.⁶ However, in patients with major ischemic strokes, acute post-event SBP was much closer to premorbid values to which these patients were presumably accustomed, with no rise in SBP before the event and only a small post-event increment.⁵ These findings suggest that the acute rise in BP mainly reflects premorbid hypertension rather than a stroke-specific response.⁵ Whether the additional small post-event increment in SBP is a direct consequence of the stroke that serves to enhance perfusion of the penumbra over collaterals is a matter of debate. Additional factors such as headache, urine retention, infection, or the psychological stress of admission to hospital could also play a role.

Should Elevated BP in Acute Stroke Be Lowered?

Several trials have assessed the question, whether BP should be lowered in patients with acute stroke, given the worse outcome in patients with high BP levels. Although there is good evidence that early BP lowering is safe and might be beneficial in patients with ICH, BP-lowering trials in patients with ischemic stroke were either neutral or negative.⁷⁻¹² There are several explanations why BP lowering in patients with ischemic stroke has not been beneficial: the lack of benefit and potential harm may be related to reducing BP to a level to which the patient is unaccustomed.⁵ In accustomed hypertension, the cerebral perfusion curve is shifted to the right, such that rapid BP lowering could compromise blood flow at a time when perfusion is already compromised.^{5,13} Furthermore, in ischemic stroke with persistent vessel occlusion lowering of BP is likely to decrease collateral flow. Because BP autoregulation is disturbed, BP lowering would reduce penumbral perfusion, which could accelerate loss of penumbral tissue and increase the core of the infarct rapidly. When the penumbra disappears, either because it is salvaged after reperfusion or because it is gradually lost into the growing infarct core while occlusion persists, elevated BP is no longer needed. This hypothesis is supported by the observation of declining BP after stroke. The pace of BP decline is faster in patients after successful recanalization of large-vessel occlusions when compared with patients with persistently blocked arteries.¹⁴

Should BP Be Lowered Before IVT?

In patients with stroke undergoing IVT, it is common practice to avoid SBP >185 mm Hg and diastolic BP >110 mm Hg. BP thresholds for IVT candidates were established during the NINDS pilot study (National Institute of Neurological Disorders and Stroke) and are based on thrombolysis databases showing baseline hypertension as a risk factor for parenchymal hemorrhage.^{1,15} Furthermore, there is an association of elevated BP levels with the reduced likelihood of recanalization in patients with stroke treated with IVT.¹⁶ However, data on BP lowering before IVT are conflicting. Two studies suggest that hypertensive patients receiving IVT and antihypertensives have a worse outcome than patients without antihypertensives.^{17,18} On the contrary, observational data suggest that BP lowering before IVT, even using aggressive measures, may not be associated with a poor outcome.¹⁹ Furthermore, in the International Stroke Trial 3, the association between BP and outcome or occurrence of ICH was not affected by IVT.²⁰ Overall, the evidence in current guidelines that advocate effective BP control before and during recombinant tissue-type plasminogen activator infusion is weak.²¹ Further trials are required to address this question more reliably.

What Is the Best BP Management Before, During, and After EVT?

Even though Mulder et al¹ have shown that the effectiveness of EVT is similar in the entire range of baseline BP, this study does not answer the question whether elevated BP before, during, or after EVT should be lowered.¹ Goyal et al²² have shown that higher admission SBP is an independent predictor of increased final infarct volume and a lower likelihood of favorable functional outcome in patients with large-vessel occlusion treated with EVT. However, given the overall poor evidence of BP management in patients with ischemic stroke and given the pathophysiological considerations mentioned above, active BP lowering in acute stroke patients with proximal vessel occlusion before recanalization might be harmful. We are therefore rather conservative and treat in the acute stroke phase only extremely high and extremely low BP. The average patient deserves careful BP observation and treatment only of persisting hypertension after the acute phase of stroke.

Although there is increasing evidence that IVT and EVT are beneficial in patients with stroke irrespective of admission BP, further studies should address the optimal BP management before, during, and after thrombolysis and thrombectomy. Such trials should focus on selected patients with low or extremely high BP and by no means lump together all patients with acute stroke.

Disclosures

None.

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