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COMMENT

Three rules for blood pressure management in acute intracerebral hemorrhage: fast, intense and stable

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Up to the early 2010s, guidelines for the management of intracerebral hemorrhage (ICH) recommended blood pressure (BP)-lowering treatment when systolic BP was >180 mm Hg [1]. In 2013, the INTERACT-2 trial provided evidence showing the benefits and safety of intensive BP lowering with target systolic BP levels of <140 mm Hg in acute ICH [2]. INTERACT-2 was a randomized, open-treatment, blinded-endpoint trial. A total of 2839 patients with CT-confirmed ICH, elevated systolic BP (150–220 mmHg), and the capacity to commence BP lowering within 6 h of onset were randomly assigned to intensive lowering of BP using routine intravenous agents (target systolic BP < 140 mm Hg) or guideline-based management of BP (target systolic BP < 180 mm Hg). Intensive BP lowering attenuated hematoma growth at 24 h in cases of acute intracerebral hemorrhage: the difference in hematoma expansion between randomized groups was 1.4 ml. Intensive BP lowering was also associated with a reduced risk of death or major disability (modified Rankin Scale [mRS] 3–6) at 90 days: 52.0% in the intensive-treatment group compared with 55.6% in the standard-treatment group (odds ratio 0.87, 95% confidence interval [CI] 0.75–1.01), although the statistical significance of the association was marginal ($P = 0.06$). In 2016, the results of the ATTACH-2 trial were reported [3]. The ATTACH-2 trial investigated the effects of intensive BP lowering with a target systolic BP of 110–139 mm Hg using continuous intravenous infusion of nicardipine among 1000 patients with acute ICH. However, there were no clear differences in rates of death/major disability (mRS 4–6) between the intensive BP lowering group and the control group (relative risk 1.04, 95% CI 0.85–12.7). The discrepancy between INTERACT-2 and ATTACH-2 might be attributable in part to differences in achieved systolic BP levels in the intensive group (average 140 mm Hg in INTERACT-2 and 120 to 125 mm Hg in ATTACH-2) because the benefits/harms of BP lowering < 130 mm Hg are not yet clear. A systematic review and meta-analysis of individual patient data did not provide a definite conclusion on the benefits/harms of BP lowering in acute intracerebral hemorrhage [4]. Based on the totality of the evidence, current guidelines recommend target systolic BP levels of <140 mm Hg for patients with acute ICH [5, 6].

In this issue of *Hypertension Research*, Toyoda K et al., using individual participant data from ATTACH-2 and SAMURAI-ICH, demonstrated the association of systolic BP levels with hematoma expansion and death/major disability (mRS 4–6) at 3 months among Japanese patients with acute ICH who received intravenous nicardipine [7]. In the present study, higher systolic BP levels on treatment were clearly associated with higher risks of hematoma expansion and death/disability. The lowest risks of adverse outcomes were observed among ICH patients who achieved systolic BP levels of <127.5 mm Hg and/or 127.5 to 134.3 mm Hg. These findings were consistent with our results from INTERACT-1 and 2, which demonstrated that the lowest risks of hematoma expansion and death/major disability (mRS 3–6) occurred among patients who achieved on-treatment systolic BP levels of 130 to 140 mm Hg [8, 9]. Based on the findings above, the optimal target systolic BP level in acute ICH seems to be approximately 130 mm Hg among Japanese individuals as well as people in other regions of the world. Among patients with acute ICH, target systolic BP < 140 mm Hg (130 mm Hg if possible) should be achieved as soon as possible (Table 1).

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Table 1 Three rules for blood pressure management in acute intracerebral hemorrhage

Rules	
1. Fast	Initiate BP lowering treatment using intravenous infusion ASAP
2. Intense	Achieve target systolic BP < 140 mm Hg (130 mm Hg if possible) ASAP
3. Stable	Keep stable control of systolic BP

BP blood pressure, *ASAP* as soon as possible

Another key factor to consider in BP management in acute ICH is time from onset to BP-lowering treatment. In a subgroup analysis from INTERACT-1, we demonstrated that reductions in absolute hematoma expansion produced by randomized intensive BP-lowering treatment over 72 h decreased progressively with delays in initiation of study treatment: 6.5 ml, 3.3 ml, 0.9 ml and 0.6 ml for quartile groups defined by time from onset to randomization of <2.9, 2.9–3.6, 3.7–4.8 and ≥4.9 h, respectively [10], suggesting that earlier initiation of intensive BP-lowering treatment provides greater protection against hematoma expansion in acute ICH. Among patients with acute ICH, BP-lowering treatment using intravenous infusion should be initiated as soon as possible after presentation to the emergency room (Table 1).

The third key factor to consider in BP management in acute ICH is BP stability. In a post hoc analysis of INTERACT-2, we found a clear association between increased variability in systolic BP during the first 7 days from onset and an increased risk of death/major disability (mRS 3–6) at 3 months [11], suggesting that the benefits of early BP lowering might be enhanced by stable control of BP. Among patients with ICH, BP stability should be considered (Table 1).

In summary, three rules of BP management (fast, intense and stable) (Table 1) should be considered for patients with acute ICH in order to provide maximal protection against hematoma expansion and subsequent poor prognosis.

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