INTERACT 2

Acute Cerebral Hemorrhage Trials (INTERACT 1 and 2).

Elevated blood pressure (BP) is a strong predictor of poor outcome in both intracerebral hemorrhage (ICH) and subarachnoid hemorrhage(SAH). Data from a landmark clinical trial INTERACT 2, wherein 2839 participants enrolled with spontaneous ICH were randomly assigned to receive intensive (target systolic BP <140 mmHg) or guideline recommended BP lowering therapy (target systolic BP <180 mmHg), showed that intensive BP lowering was safe, and more favorable functional outcome and better overall health-related quality of life were seen in survivors in the intensive treatment group. These results contributed to the shift in European and American guidelines towards more aggressive early management of elevated BP in ICH. In contrast, the treatment of BP in SAH is less well defined and more complex. Although there is consensus that hypertension needs to be controlled to prevent rebleeding in the acute setting, induced hypertension in the later stages of SAH has questionable benefits [1)].

The Second Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT 2) study, a multinational, multicenter, randomized controlled trial published in 2013, demonstrated better functional outcomes with no harm for patients with acute spontaneous intracerebral hemorrhage (ICH) within 6 h of onset who received target-driven, early intensive BP lowering (systolic BP target <140 mmHg within 1 h, continued for 7 days) and suggested that greater and faster reduction in BP might enhance the treatment effect by limiting hematoma growth. The trial resulted in revisions of guidelines for acute management of ICH, in which intensive BP lowering in patients with acute ICH is recommended as safe and effective treatment for improving functional outcome. BP lowering is also the only intervention that is proven to reduce the risk of recurrent ICH.

INTERACT2 was an international, open, blinded end point, randomized controlled trial of patients with spontaneous intracerebral hemorrhage (<6 hours) and elevated systolic blood pressure (SBP) (150-220 mm Hg) assigned to intensive (target SBP <140 mm Hg) or guideline-recommended (SBP <180 mm Hg) treatment.

Associations of BP reduction (baseline minus average of achieved SBP) during 3 time periods post randomization (15-60 minutes, 1-24 hours, and 2-7 days) on poor outcome (death or major disability) at 90 days were analyzed in multivariable logistic regression models with odds ratios and 95% confidence intervals. Larger SBP reductions within the first hour after randomization were associated with lower risks of poor outcome: compared with minimal reduction (<10 mm Hg), odds ratios were 0.80 (95% confidence interval, 0.63-1.02) for moderate (10-20 mm Hg) and 0.65 (0.52-0.82) for large (≥20 mm Hg) reductions (P trend <0.01). Similar associations were also observed for SBP reductions during 1 to 24 hours (P<0.01) and 2 to 7 days (P 0.02). No heterogeneity in associations for patients above or below baseline SBP 180 mm Hg was reported (P>0.30). Optimal recovery from intracerebral hemorrhage was observed in hypertensive patients who achieved the greatest SBP reductions (≥20 mm Hg) in the first hour and maintained for 7 days [2)].

Current evidences from several randomized trials, including PROGRESS and SPS3, indicate that long-term strict BP control in patients with ICH is safe and could offer additional benefits in major reduction in risk of recurrent ICH. The latest American Heart Association/American Stroke Association (AHA/ASA) guidelines recommended a target BP of <130/80 mmHg after ICH, but supporting evidence is limited. Randomized controlled trials are needed that focus on strict BP control, initiated early after onset of

the disease and continued long-term, to demonstrate effective prevention of recurrent stroke and other major vascular events without additional harms in the ICH population [3].

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