

Critical Review Form

Meta-analysis

[Tsivgoulis G, Katsanos AH, Butcher KS, Boviatsis E, Triantafyllou N, Rizos I, Alexandrov AV. Intensive blood pressure reduction in acute intracerebral hemorrhage: a meta-analysis. Neurology. 2014 Oct 21;83\(17\):1523-9.](#)

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ives: "to confirm INTERACT II findings by conducting a systematic review and meta-analysis on the safety and efficacy of intensive BP reduction (beyond the levels recommended by AHA guidelines) in patients with acute ICH, using all available RCT data." (p. 1524)

Methods: Two authors searched MEDLINE, the CENTRAL Register of Controlled Trials, and the Cochrane Database of Systematic Reviews database (last search on February 23, 2014) to identify eligible randomized controlled trials (RCTs) reported efficacy and safety of intensive BP reduction in acute ICH. Studies were eligible for inclusion if they were RCTs enrolling patients with symptom onset < 24 hours prior to randomization and compared intensive BP reduction to standard or guideline-based BP management.

Included studies were assessed for bias by three reviewers using the [Cochrane Collaboration tool for assessing risk of bias](#) in randomized trials. Two independent authors abstracted data on efficacy and safety for both intensive and guideline-based therapy groups. Disagreement was settled by consensus. The primary efficacy outcome being analyzed was death or disability at 3 months, defined as a [modified Rankin Scale](#) (mRS) score > 2. The primary safety outcome was 3-month mortality. Available data on hematoma growth at 24 hours was also extracted. Data was pooled using a [random effects model](#).

The MEDLINE search yielded 71 results, of which 7 were potentially eligible. Searching the CENTRAL Register of Controlled Trials, and the Cochrane Database of Systematic Reviews database identified no additional studies. Two studies were excluded because they included patients with ischemic stroke, and an additional study was excluded because it was not a randomized trial. A total of 4 studies were included in the meta-analysis with a total of 3315 participants (mean age 63.8 years; 63.7% men).

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Yes. The authors wished to determine whether more aggressive BP reduction would benefit patients with spontaneous ICH compared to standard or "guideline-based" BP control. There is some concern that elevated

		BP can lead to increased bleeding and hematoma volume while more intensive lowering of BP could result in decreased cerebral blood flow.
2.	Was the search for relevant studies detailed and exhaustive?	No. The authors searched MEDLINE, the CENTRAL Register of Controlled Trials, and the Cochrane Database of Systematic Reviews database, and did also search reference lists of eligible articles and of relevant review articles, but they did not search relevant EMBase, the Web of Science, SCOPUS, conference proceeding abstracts, or the gray literature .
3.	Were the primary studies of high methodological quality?	Yes. Overall, the studies were of high methodological quality with a low risk of bias. All of the studies were open-label with blinding of outcome assessors and one of the studies (Koch 2008) did not clearly state the randomization method.
4.	Were the assessments of the included studies reproducible?	Yes and no. While the authors used a well-validated system for evaluating risk of bias, they did not document the results of their assessment. They note that these assessments are in table e-3, but this table is nowhere in the paper or online for review.
II.	<i>What are the results?</i>	
1.	What are the overall results of the study?	<ul style="list-style-type: none"> • For the primary outcome of interest (mRS > 2) there was no statistically significant difference between patients in the intensive BP-lowering group and the standard care group: OR 0.87, 95% CI 0.76-1.01. • There was no difference in mortality between the groups: OR 1.01, 95% CI 0.83-1.23. • Intensive BP reduction was associated with a greater attenuation of absolute hematoma growth at 24 hours (standardized mean difference \pm SE: -0.110 \pm 0.053; p = 0.038) in comparison to standard BP reduction.
2.	How precise are the results?	See above. The confidence intervals are fairly narrow, though for the primary outcome it should be noted that they barely cross 1.0.
3.	Were the results similar from study to study?	For the efficacy outcomes (mRS > 2 and mortality) there was no detectable heterogeneity, with an I ² of 0% in both instances and p values of 0.723 and 0.876, respectively.
III.	<i>Will the results help me in caring for my patients?</i>	
1.	How can I best interpret the results to apply them to the care of my patients?	In patients with acute spontaneous ICH with symptom onset < 24 hours prior to presentation, more intensive BP management (typically a goal SBP < 140 mmHg) does not appear to improve clinically relevant outcomes when compared to more traditional guideline-based BP

		management. This conclusion is somewhat limited by the lack of an exhaustive literature search and some clinical heterogeneity between studies.
2.	Were all patient important outcomes considered?	Mostly yes. The authors considered the most clinically relevant outcomes (functional status, mortality) but did not consider quality of life, length of stay, or cost.
3.	Are the benefits worth the costs and potential risks?	Likely no. Based on this data, there is no clear benefit to more intensive BP lowering compared to standard guideline-based BP management.

Limitations:

1. Very little clinical information is provided regarding
2. The authors report that there is no [publication bias](#). However, there were only 4 studies included in the meta-analysis, hence it would not be possible to accurately assess for publication bias.
3. The authors did not perform a very thorough literature search. They did not search EMBase, the Web of Science, SCOPUS, conference proceeding abstracts, or the [gray literature](#).
4. While the authors used a well-validated system for evaluating risk of bias, they do not provide the results of their assessment anywhere that can be easily found.

Bottom Line:

This systematic review of RCTs found no statistically significant improvement in functional status with intensive blood pressure lowering compared to standard BP management strategies in spontaneous intracerebral hemorrhage (OR for having a mRS > 2 of 0.87, 95% CI 0.76-1.01). This finding confirms the results of the individual trials. While the authors did not perform an exhaustive search of the literature, it is unlikely that any large, methodologically sound studies were missed.