

The INTERACT 2 study

Summary by Dr. Teresa Chan Reviewed by Dr. Patrick Archambault & Dr. Tim Chaplin.

Topic	Neurology								
Citation of Paper:	Anderson, C. S., Heeley, E., Huang, Y., Wang, J., Stapf, C., Delcourt, C., ... & Chalmers, J. (2013). Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. <i>New England Journal of Medicine</i> , 368(25), 2355-2365. (INTERACT-2) LINK: http://www.nejm.org/doi/full/10.1056/NEJMoa1214609								
Clinical Question:	Does rapid lowering of elevated blood pressure improve the outcome in patients with intracerebral haemorrhage?								
PICO	<table border="1"> <tr> <td>P:</td> <td>2839 patients who had: 1) spontaneous intracerebral haemorrhage within the previous 6 hours; AND 2) Elevated Systolic BP (i.e. BP between 150-220 mmHg)</td> </tr> <tr> <td>I:</td> <td>Lower BP to target systolic level of < 140 mmHg within 1 hour with agents of physician's choosing</td> </tr> <tr> <td>C:</td> <td>Lower BP to target systolic level of < 180 mmHg (per guidelines) with agents of physician's choosing</td> </tr> <tr> <td>O:</td> <td>Primary Outcome: Death or Major Disability (modified Rankin score of 3-6) at 90 days</td> </tr> </table>	P:	2839 patients who had: 1) spontaneous intracerebral haemorrhage within the previous 6 hours; AND 2) Elevated Systolic BP (i.e. BP between 150-220 mmHg)	I:	Lower BP to target systolic level of < 140 mmHg within 1 hour with agents of physician's choosing	C:	Lower BP to target systolic level of < 180 mmHg (per guidelines) with agents of physician's choosing	O:	Primary Outcome: Death or Major Disability (modified Rankin score of 3-6) at 90 days
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Methods	Multicenter, Randomized Controlled Study. Open Label (Unblinded); Physician-choice intervention Analysis with Intention-to-treat principle								
Results	719 of 1382 patients (52%) of those receiving intensive treatment vs. 785 of 1412 (55.6%) patients in guideline-targets had the primary outcome. Odds ratio with intensive treatment 0.87; 95% CI, 9.75-1.01; p=0.06 Bimodal ("Ordinal") analysis of the patients stratifying them by their modified Rankin Score yielded a significant difference (p=0.04) between the intensive vs. guideline-recommended targets. (See Table 3 in the paper).								
Conclusion	Conclusion verbatim from study: "In patients with intracerebral haemorrhage, intensive lowering of blood pressure did not result in a significant reduction in the rate of the primary outcome of death or severe disability. An ordinal analysis of modified Rankin scores indicated improved functional outcomes with intensive lowering of blood pressure."								
Take Home Point	There is no difference in ICH patients if you intensively lower their BP to targets of 140mmHg vs. the guidelines-suggested target of 180 mmHg. There may be some interaction between BP targets and severity of outcomes as per the modified Rankin Score, but it is unclear if there is a clinically significant difference or merely a statistical anomaly.								
Caveats	Of note, half of the patients in the guideline group had an SBP > 180mmHg at baseline, and only 303 of them received ANY anti-hypertensive agent in the first group. This is concerning since the intervention group received IV therapy quite avidly and at a significantly higher rate (p < 0.0001) The authors completed many comparisons in this study between the two groups, and the only difference in outcome they were able to find was in the ordinal comparison (which lumps several comparisons into one), and yet their significance threshold was only set at p=0.05. While the Bonferroni correction is likely too conservative in its adjustments, some sort of correction for the number of comparisons might have been warranted. As such, it is unclear to us whether there is any clinically meaningful difference between rapidly lowering systolic blood pressure targets to 140mmHg vs. the guideline recommended 180mmHg. Predominantly the enrolment was from China as well (~60% of the patients were male patients in China).								
FOAMed Resources	EMLit of Note http://www.emlitofnote.com/2013/05/interact2-ich-half-truths.html NeuroICUdoc: http://www.neuroicudoc.com/2013/06/blood-pressure-reduction-for.html The SGEM: http://thesgem.com/2014/05/sgem73-how-low-can-you-go-lowering-bp-in-ich/								

