

**Journal Club Eastern Virginia Medical School**  
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CITATION: Anderson CS, Huang Y, Wang JG, Arima H et al. Intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT): a randomised pilot trial. Lancet Neurol. 2008 Apr 4; PMID: 18396107.

I. WHAT IS BEING STUDIED?	INTENSIVE LOWERING OF BP (TARGET SYSTOLIC BP 140 MM HG) OR STANDARD GUIDELINE-BASED MANAGEMENT OF BP (TARGET SYS BP 180 MM HG)
1. Study Objective	The primary endpoint: proportional change in hematoma volume at 24 h  Secondary outcomes: other measurements of hematoma volume, clinical outcomes.
2. Study Design	Investigator-initiated, multicenter, open, blinded outcome, randomized trial in 44 hospitals in 3 countries
3. Inclusion Criteria	18 years of age  spontaneous ICH confirmed by CT and elevated systolic blood pressure (150–220 mm Hg)  Ability to commence the treatment within 6 h of onset in a monitored environment.
4. Exclusion Criteria	systolic blood pressure >220 mm Hg or hypertensive encephalopathy  Contraindication to intensive lowering of blood pressure (severe cerebral artery stenosis or renal failure)  ICH secondary to a structural cerebral abnormality (avm, intracranial aneurysm, or tumor)  use of a thrombolytic agent or an ischemic stroke within 30 days  GCS of 3–5. Significant prestroke disability or medical illness  Decompressive neurosurgical intervention
5. Interventions Compared	Early intensive BP reduction a systolic blood pressure of 140 mm Hg within 1 h for the next 7 days versus

	standard guideline-based management of BP (target systolic BP 180 mm Hg. Both oral and IV antihypertensives used . CT scanning at baseline, 24 h and 72 h.
6. Outcomes Evaluated	<p>Primary endpoint was the proportional change or growth in hematoma volume in 24 h</p> <p>Secondary outcomes: absolute and substantial growth of the hematoma plus any intraventricular hemorrhage.</p> <p>Substantial growth = increase in volume of more than 33% or more than 12.5 mL in the first 24 h.</p> <p>The clinical endpoint: combination of death and dependency (mRS score of 3–5) at 90 days. GCS, NIHSS, modified Rankin scale, Barthel index, MMSE, EuroQol 5D</p>
<b>II. Are the results of the study valid?</b>	
1. Was the assignment of patients randomized?	Yes. Via an internet-based system, with patients stratified according to country of residence and time from onset of ICH (<3 h vs >3 h).
2. Were all patients who entered the trial properly accounted for and attributed at its conclusions?	Yes.
3. Was follow-up complete?	Yes, at 90 days 1 pt in each group was lost to follow up. 6 in control and 3 in treatment group but unable to do clinical scales
4. Were patients, health workers and study personnel “blind” to treatment?	Health care workers were aware of treatment arm, however, CT scans were read by 2 neurologists independently who were blinded to clinical data. Initial clinical scales and follow up 28d and 90d done by different investigator to assist blinding.
5. Were study groups similar at the start of the trial?	Yes.
6. Aside from the experimental intervention, were the groups treated equally	Yes.
<b>III. What were the results?</b>	
1. How large was the treatment effect?	intensive group showed significantly lower mean Proportional hematoma growth at 24 h (22.6% at 0.04)

(difference between treatment and control group).	<p>was not significant after adjustment for initial volume and time from ICH onset to CT (10% at 0.06).</p> <p>Substantial hematoma growth and mean absolute increase in hematoma volume were smaller in the intensive group but not significant</p>
2. What was the estimated treatment effect at a 95% confidence interval?	<p>Risk reduction of substantial hematoma growth 36% (0-59% interval)</p>
IV. Will the results help me in caring for my patients? (applicable ?)	<p>Yes, however, not yet. The study was not large enough to correlate hematoma growth with clinical outcomes of disability as it is only scouting trial. It is hard to say if these minor decreases in hematoma growth at this time will correlate with less overall dysfunction.</p>
1. Were all clinically important outcomes considered?	<p>Yes, however as above, not powered enough to make a correlation</p>
2. Are treatment outcomes worth the potential harms?	<p>Yes, as blood pressure control is an easy modifier, however, potential to harm has not been assessed with either guideline vs aggressive treatment in good clinical studies.</p>

Additional Comments:

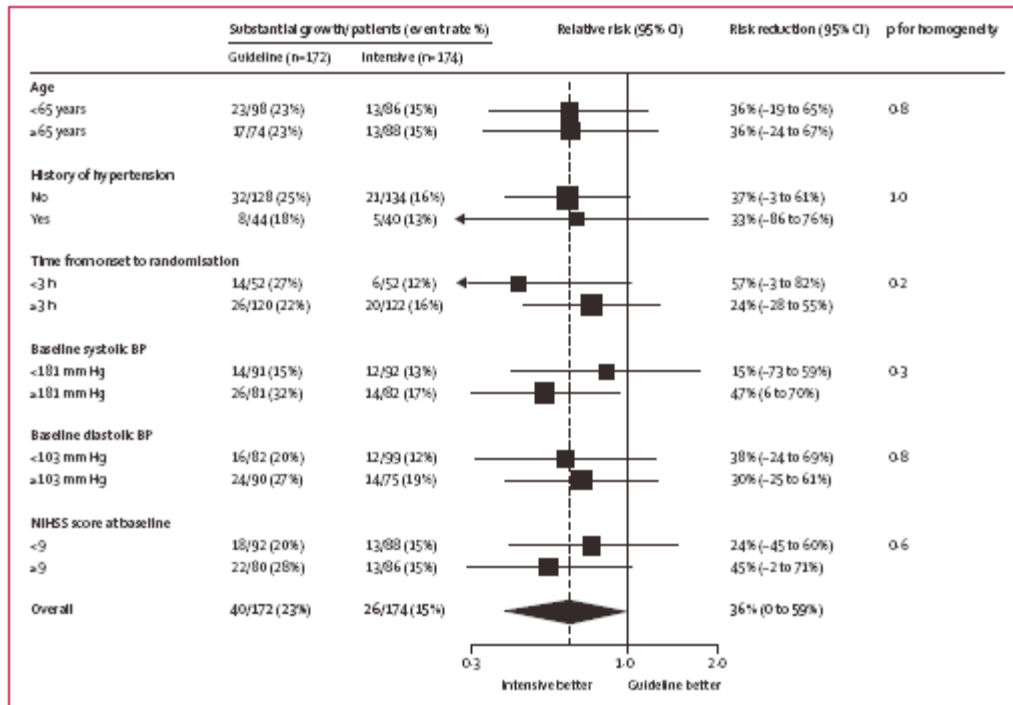


Figure 3: Effect on substantial haematoma growth in predefined subgroups

	Guideline (n=172)	Intensive (n=174)	Difference (95% CI)*	p
<b>Haematoma</b>				
Mean baseline volume (mL)	12.7 (11.6)	14.2 (14.5)	-	-
Mean volume at 24 h (mL)	15.4 (14.7)	15.2 (17.5)	-	-
Proportional increase (%)				
Mean (95% CI)	36.3% (15.8 to 56.8%)	33.7% (5.9 to 21.5%)	22.6% (0.6 to 44.5%)	0.04
Adjusted median (95% CI)†	16.2% (8.8 to 24.1%)	6.2% (-0.7 to 13.4%)	10.0% (0.0 to 20.5%)	0.06
Absolute increase (mL)				
Mean (95% CI)	2.7 (1.4 to 4.0)	0.9 (-0.9 to 2.7)	1.7 (-0.5 to 4.0)	0.12
Adjusted mean (95% CI)	2.6 (1.1 to 4.2)	0.9 (-0.6 to 2.5)	1.7 (-0.5 to 3.9)	0.13
Substantial growth‡	40 (23%)	26 (15%)	8% (-1.0 to 17.0%)§	0.05
<b>Haematoma plus IVH</b>				
Mean baseline volume (mL)	16.2 (16.1)	16.2 (17.1)	-	..
Mean volume at 24 h (mL)	19.2 (20.4)	17.6 (20.2)	-	..
Proportional increase (%)				
Mean (95% CI)	40.2% (17.6 to 62.8%)	17.3% (5.8 to 28.8%)	22.9% (-2.5 to 48.2%)	0.08
Adjusted median (95% CI)†	17.6% (10.1 to 25.5%)	7.6% (0.8 to 14.9%)	10.0% (0.0 to 20.8%)	0.06
Absolute increase (mL)				
Mean (95% CI)	3.1 (1.0 to 5.2)	1.4 (-0.4 to 3.2)	1.7 (-1.1 to 4.5)	0.23
Adjusted mean (95% CI)	3.1 (1.2 to 5.1)	1.3 (-0.6 to 3.3)	1.8 (-1.0 to 4.5)	0.21
Substantial growth‡	38 (22%)	26 (15%)	7% (-2.0 to 16.0)¶	0.07

Data are n (%) or mean (SD) except where indicated. Proportional and absolute changes were calculated by ANCOVA and substantial growth by logistic regression. 95% CI for the differences in adjusted medians were calculated using the bootstrap percentile method. †Adjustments were made for baseline volume of haematoma and time from onset of ICH to CT scan. IVH=intraventricular haemorrhage. Some increases and differences do not equal the differences between data presented here because of rounding to one decimal place. \*Differences between groups. †Because of skewed raw data, adjusted medians are reported with 95% CI obtained by back-transformation. ‡An increase in haematoma volume of >33% or >12.5 mL during the first 24 h after ICH onset. §Relative risk reduction 36% (95% CI 0 to 59). ¶Relative risk reduction 32% (95% CI -6 to 57).

Table 3: Effects of early treatment to lower blood pressure on haematoma growth