Hyperacute BP management of AIS and ICH in Neurocritical Care: The evidence and unresolved issues

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Disclosures

- None
Objectives

I. Introduction and delineation of the problems

II. Cerebral autoregulation in AIS and ICH

III. Hyperacute BP management in AIS

IV. Hyperacute BP management in ICH
Introduction and the current controversies

- 60%-70% of stroke patients present with SBP > 140.

- Transient Htn is seen in > 60% patients after ischemic stroke and its proper Treatment remains unclear.

- BP management in stroke has been controversial and remains a matter of debate.

- To treat or not to treat? How fast? How low should we go?

- Failure of every large trial to provide a definitive answer.

- High BP is associated independently with poor outcome in AIS (early recurrence or death)

- High BP is related to hematoma expansion and worse functional outcome after ICH.
Conundrums

- A certain degree of BP lowering might be required but the **optimal target level** and rapidity of BP reduction has not clearly been identified.

- Pathophysiological concerns are based on the presence of **dysfunctional cerebral autoregulation** with lowering BP will reduce tissue perfusion and increase lesion size thereby worsen outcome.

- Most large sized trials comparing active lowering of BP with no or guidelines based lowering have been **neutral** or **negative**.

- **Limitation of these studies**: few critically ill patients with severe AIS or ICH were included in trials those are the patients particularly prone to inadequate cerebral perfusion and most dependent on optimal BP control.

- Effects on outcome probably depend on which sort of stroke is being treated, how and when BP is lowered.
<table>
<thead>
<tr>
<th>Trial</th>
<th>Intervention Class (Agent)</th>
<th>Size</th>
<th>CTR (%)</th>
<th>Result/Comment(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH-1</td>
<td>ARA (trandolapril po)</td>
<td>274</td>
<td>&lt;30</td>
<td>Negative</td>
</tr>
<tr>
<td>INTERACT</td>
<td>Intensity, multiple classes: a- AA (urapidil IV, fenofibrate) 63%; loop diuretic (furosemide) 35%; NO donor (nitroglycerine) 13%</td>
<td>404</td>
<td>&lt;6</td>
<td>Neutral</td>
</tr>
<tr>
<td>INTERACT-2</td>
<td>Intensity, multiple classes: a- AA (urapidil IV) 32.5%; NO donor (nitroglycerine, nitroprusside) 27.6%; CBB (nicardipine) 16.2%; combined a- AA/β-RA (labelotral) 14.4%; diuretic (furosemide) 12.4%</td>
<td>2794</td>
<td>&lt;6</td>
<td>Neutral; positive on ordinal analysis</td>
</tr>
<tr>
<td>ATACH-2</td>
<td>CBB (nicardipine IV)</td>
<td>1000</td>
<td>&lt;4.5</td>
<td>Neutral</td>
</tr>
<tr>
<td>INTERACT-3 bundle</td>
<td>Intensity, multiple classes: (glucose and temperature control, and reversal of anticoagulation)</td>
<td>≈6621</td>
<td>&lt;6</td>
<td>Ongoing</td>
</tr>
<tr>
<td>ICH-ADAPT-2</td>
<td>Intensity using labelotral, hydralazine,enalapril</td>
<td>≈2/0</td>
<td>&lt;6</td>
<td>Ongoing</td>
</tr>
<tr>
<td>IS</td>
<td>Bridgers et al.</td>
<td>204</td>
<td>&lt;24</td>
<td>Negative tendency</td>
</tr>
<tr>
<td>INVEST</td>
<td>CBB (nimodipine IV)</td>
<td></td>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>CATIE</td>
<td>ACE (enalapril IV) then CBB then diuretic</td>
<td>4071</td>
<td>&lt;24</td>
<td>Neutral</td>
</tr>
<tr>
<td>(SCAST-1)</td>
<td>ARA (trandolapril po)</td>
<td>358</td>
<td>&lt;30</td>
<td>Neutral</td>
</tr>
<tr>
<td>VENTURE</td>
<td>ARA (valsartan po)</td>
<td>383</td>
<td>&lt;48</td>
<td>Neutral</td>
</tr>
<tr>
<td>ENCHANTED BP</td>
<td>Intensity (mainly a AA, urapidil IV)</td>
<td></td>
<td></td>
<td>Ongoing</td>
</tr>
<tr>
<td>Menuet</td>
<td>β-RA (atenolol, propranolol po)</td>
<td>362</td>
<td>&lt;48</td>
<td>Negative</td>
</tr>
<tr>
<td>SCAST</td>
<td>ARA (trandolapril po)</td>
<td>2029</td>
<td>&lt;30</td>
<td>Neutral; negative if recurrence coronary ignored</td>
</tr>
<tr>
<td>ENCS</td>
<td>NO donor (NTG bd)</td>
<td>4011</td>
<td>&lt;40</td>
<td>Neutral</td>
</tr>
<tr>
<td>(ENOS early)</td>
<td>NO donor (NTG bd)</td>
<td>273</td>
<td>&lt;5</td>
<td>Positive</td>
</tr>
<tr>
<td>RIGHT-2</td>
<td>NO donor (NTG bd)</td>
<td>≈1105</td>
<td>&lt;4</td>
<td>Ongoing</td>
</tr>
<tr>
<td>MR-ASAP</td>
<td>NO donor (NTG bd)</td>
<td>≈1400</td>
<td>&lt;3</td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

Medium and Large Randomized Controlled Trials of Blood Pressure Lowering in Acute Stroke.
I. Cerebral Autoregulation (CA)

- Mechanism that maintains constant cerebral blood flow (CBF) regardless of change in Cerebral perfusion pressure (CPP) or mean arterial pressure (MAP)
- CPP is the difference in the pressure between the arterial and venous circulation which dictates the blood flow in the brain.
- CPP is affected by ICP (another pressure within the skull) by this relationship:
  \[ \text{CPP} = \text{MAP} - \text{ICP} \]
- In normal adult CPP is 70-90 mmHg and CBF is constant. CPP < 50 increases risk of brain ischemia.
- When CA is intact, a drop in CPP may induce cerebral vasodilatation via decrease in vascular resistance to maintain constant CBF.
- It is believed to occur via myogenic mechanism whereby an increase in MAP increases the transmural tension causing depolarization of smooth muscles and constriction of precapillary resistance vessels. The reverse happens when the MAP decreases. This occurs between MAP of 50-150 mmHg.
Cerebral autoregulation maintains a constant cerebral blood flow (CBF) over a wide range of cerebral perfusion pressure (CPP) from 50 to 140 mmHg (solid line) by altering vascular resistance (represented by circles). Following brain injury autoregulation may be completely lost resulting in a linear relationship between CPP and CBF (dashed line).
Cerebral Autoregulation

- It is an almost instant process (1-3 s of change of pressure) and mediated primarily by an Endothelium Derived relaxing factor and NO (EDRF/NO).

- An increase in MAP $>150$ mmHg may lead to forced dilatation and cerebral Hyper perfusion.

- A drop in MAP $< 50$ mm Hg results in passive vessels collapse and ischemia secondary to Hypoperfusion.

- CA is believed to be altered and defective in patient with severe stroke. CBF become pressure-dependent and directly change with change in MAP. Any abrupt BP drop could lead to a drop in CBF predisposing to cerebral ischemia.
CA dysfunction in AIS.

- In LVO an elevated BP may return to baseline after complete recanalization suggesting that BP elevation is closely linked to brain tissue ischemia.

- BP elevation by itself beneficial in augmenting CBF in the penumbra in AIS.

- Rapid spontaneous decrease of BP may reflect less severe stroke, recanalization of the vessel or might be due to cardiac insufficiency all of which have an independent effect on outcome. So it might be a sign for rapidly resolving or rapidly deteriorating process.
BP and Outcome in AIS

There is a **U-shaped** relationship between presenting BP and outcome after ischemic stroke.

Both low and high extremes of BP are associated with a poor outcome.

For every 10mmHg of **SBP below 150mmHg** the risk of early death increased by 3.6%, the risk of late death and dependency increased by 17.9%

The best outcomes were observed in patients with systolic BP 150–160 mmHg
lower risk of death and dependency observed with baseline SBP 140-170.

Hyperacute BP management in AIS

- First, it is a **Balancing Act!!** Penumbra perfusion against risk of reperfusion injury and HT.

- In almost all cases of acute neurological illness, systemic HTN is a reflex response to a decrease in CPP.

- Clinical and experimental evidence indicates that reduction in BP carry a risk of producing further ischemic brain damage.

- In the absence of hypertensive encephalopathy or systemic cardiovascular issues requiring immediate BP reduction (AMI, ACS, Ao dissection) **the benefits** from immediately or acutely lowering BP in AS on any kind remain conjunctural and unsupported by strong validated evidences.

- At present **No convincing evidence** that BP reduction results in improved outcomes for patients with AIS.
What is the 2018 ASA/AHA guidelines say?

<table>
<thead>
<tr>
<th>3.2. Blood Pressure</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hypotension and hypovolemia should be corrected to maintain systemic perfusion levels necessary to support organ function.</td>
<td>I</td>
<td>C-EO</td>
<td>New recommendation.</td>
</tr>
</tbody>
</table>

The blood pressure (BP) level that should be maintained in patients with AIS to ensure best outcome is not known. Some observational studies show an association between worse outcomes and lower BPs, whereas others have not. No studies have addressed the treatment of low BP in patients with stroke. In a systematic analysis of 12 studies comparing colloids with crystalloids, the odds of death or dependency were similar. Clinically important benefits or harms could not be excluded. There are no data to guide volume and duration of parenteral fluid delivery. No studies have compared different isotonic fluids.

| 2. Patients who have elevated BP and are otherwise eligible for treatment with IV alteplase should have their BP carefully lowered so that their systolic BP is <185 mm Hg and their diastolic BP is <110 mm Hg before IV fibrinolytic therapy is initiated. | I | B-NR | Recommendation reworded for clarity from 2013 AIS Guidelines. Class unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table LXVIII in online Data Supplement 1 for original wording. |

The RCTs of IV alteplase required the BP to be <185 mm Hg systolic and <110 mm Hg diastolic before treatment and <180/105 mm Hg for the first 24 hours after treatment. Options to treat arterial hypertension in patients with AIS who are candidates for acute reperfusion therapy are given in Table 5. Some observational studies suggest that the risk of hemorrhage after administration of alteplase is greater in patients with higher BPs and in patients with more BP variability. The exact BP at which the risk of hemorrhage after thrombolysis increases is unknown. It is thus reasonable to target the BPs used in the RCTs of IV thrombolysis.

| 4. The usefulness of drug-induced hypertension in patients with AIS is not well established. | Iib | C-LD | Recommendation and Class unchanged from 2013 AIS Guidelines. LOE revised. |
### 4.3. Blood Pressure

<table>
<thead>
<tr>
<th>1. In patients with AIS, early treatment of hypertension is indicated when required by comorbid conditions (e.g., concomitant acute coronary event, acute heart failure, aortic dissection, postthrombolysis sICH, or preeclampsia/eclampsia). Lowering BP initially by 15% is probably safe.</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>C-E0</td>
<td>New recommendation.</td>
</tr>
</tbody>
</table>

Patients with AIS can present with severe acute comorbidities that demand emergency BP reduction to prevent serious complications. However, it is important to keep in mind that excessive BP lowering can sometimes worsen cerebral ischemia.\(^{215}\) Ideal management in these situations should be individualized, but in general, initial BP reduction by 15% is a reasonable goal.

<table>
<thead>
<tr>
<th>3. In patients with BP $\geq$220/120 mmHg who did not receive IV alteplase or EVT and have no comorbid conditions requiring acute antihypertensive treatment, the benefit of initiating or reinitiating treatment of hypertension within the first 48 to 72 hours is uncertain. It might be reasonable to lower BP by 15% during the first 24 hours after onset of stroke.</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IIb</td>
<td>C-E0</td>
<td>New recommendation.</td>
</tr>
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</table>

Patients with severe hypertension (most commonly $\geq$220/120 mm Hg) were excluded from clinical trials evaluating BP lowering after AIS.\(^{218,219,222,223,225,228}\) BP reduction has been traditionally advised for these cases, but the benefit of such treatment in the absence of comorbid conditions that may be acutely exacerbated by severe hypertension has not been formally studied.

<table>
<thead>
<tr>
<th>4. Although no solid data are available to guide selection of medications for BP lowering after AIS, the antihypertensive medications and doses included in Table 5 are reasonable options.</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IIa</td>
<td>C-E0</td>
<td>Recommendation/table revised from 2013 AIS Guidelines.</td>
</tr>
</tbody>
</table>

There are no data to show that 1 strategy to lower BP is better than another after AIS. The medications and doses in Table 5 are all reasonable options.

<table>
<thead>
<tr>
<th>5. Starting or restarting antihypertensive therapy during hospitalization in patients with BF $&gt;140/90$ mm Hg who are neurologically stable is safe and is reasonable to improve long-term BP control unless contraindicated.</th>
<th>COR</th>
<th>LOE</th>
<th>New, Revised, or Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IIa</td>
<td>B-R</td>
<td>New recommendation.</td>
</tr>
</tbody>
</table>

Starting or restarting antihypertensive medications has been shown to be associated with improved control of the BP after discharge in 2 trials.\(^{223,225}\) Therefore, it is reasonable to start or restart antihypertensive medications in the hospital when the patient remains hypertensive and is neurologically stable. Studies evaluating this question included only patients with previous diagnosis of hypertension\(^{223}\) or enrolled mostly patients with previous hypertension.\(^{223}\) However, because hypertension is not uncommonly first diagnosed during the hospitalization for stroke, it is reasonable to apply this recommendation also to patients without preexistent hypertension.

See Table L in online Data Supplement 1.
BP and Thrombolysis


- When IV rt-PA is given BP should be controlled at Below 185/110 and kept or maintained below 180/105 up to 24 h post t-PA. Outcome after IV t-PA was often best at an SBP range 140-160 (but lacking recanalization status and details about BP control). Ahmed et Al: relationship of BP therapy and outcome in AIS treated with thrombolytic. Retrospective analysis SITS-ISTR Stroke 2009.

- BP threshold for IVT candidates were established during NINDS pilot study showing baseline HTN as a risk factor for parenchymal Hemorrhage, but conflicting evidence exist on BP Lowering before IVT.
BP and Thrombolysis


- When thrombolysis is not an option, best to observe current guidelines, which recommend a 15% reduction within the first 24 hours of ischemic stroke only in cases where BP exceeds 220/120 mm Hg.

- Must take into consideration the potential of compromising collateral blood flow and hastening the interval to infarction (range 6–18 hours after large vessel ischemic stroke), vs the potential for adverse systemic effects as a result of persistently elevated BP.
What is the best BP control before, during, and after Endovascular treatment (EVT).

- Benefit of EVT in LVO is clear and established (MRCLEAN, DAWN, DIFFUSE 3)

- Data regarding BP management after EVT is scant.

- **Current guidelines inadequately address BP control after EVT given lack of RCTs.**

  - **Guidelines:** BP to be maintained <185/110 for patients who have not received IVT and for whom EVT is planned (COR IIa LOE B). Keep < 180/105 after successful recanalization.

  - Many Interventional Surgeon have intuitively adopted the custom to keep SBP < 180 (as many patients may have received IVT) and to lower BP further once recanalization is achieved.
<table>
<thead>
<tr>
<th>3.7. Mechanical Thrombectomy (Continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COR</strong></td>
</tr>
<tr>
<td>17. In patients who undergo mechanical thrombectomy, it is reasonable to maintain the BP ≤180/105 mmHg during and for 24 hours after the procedure.</td>
</tr>
<tr>
<td>18. In patients who undergo mechanical thrombectomy with successful reperfusion, it might be reasonable to maintain BP at a level &lt;180/105 mmHg.</td>
</tr>
</tbody>
</table>

There are very limited data to guide BP therapy during and after the procedure in patients who undergo mechanical thrombectomy. RCT data on optimal BP management approaches in this setting are not available. The vast majority of patients enrolled in under 6-hour RCTs received IV alteplase and the trial protocols stipulated management according to local guidelines with BP ≤80/105 during and for 24 hours after the procedure for these participants. Two trial protocols provided additional recommendations. The ESCAPE protocol states that systolic BP ≥150 mm Hg is probably useful in promoting and keeping collateral flow adequate while the artery remains occluded and that controlling BP once reperfusion has been achieved and aiming for a normal BP for that individual is sensible. Labetalol or an IV β-blocker such as metoprolol in low doses is recommended. The DAWN protocol recommends maintaining systolic BP <140 mm Hg in the first 24 hours in subjects who are reperfused after mechanical thrombectomy (defined as achieving more than two thirds MCA territory reperfusion). See Table XXIII in online Data Supplement 1.
Patient with LVO are prone to BP derangement and loss of cerebral autoregulation and this is further exacerbated by periprocedural measures if patient is receiving EVT.

In the first 24 h, moderate BP goal of <160/90 was independently linked to lower mortality at 3 months compared to permissive hypertension after complete recanalization. Goyal et al: BP levels post Mechanical thrombectomy and outcome in LVO. Neurology 2017.

Given the available data, treating severe HTN after EVT with a target of keeping SBP <160 seems prudent.

This target may require adjustment after accounting for the final degree of recanalization, quality of collaterals, baseline BP, use of IVT and underlying cardiac function.
Post perfusion BP management should take into account patient baseline BP and balancing reperfusion needs against Risk of HT. (Class IIB, LOE C).

Hemodynamic support to sustain ischemic penumbra in patient with unsuccessful or partial recanalization after reperfusion therapy/EVT is essential. But it is important to limit the risk of reperfusion injury and HT.

Efforts to increase perfusion with permissive or induced HTN up to 24-48 h is likely to be helpful. It enables adaptation of collaterals to accommodate increase blood flow in poorly perfused areas. (Class IIB, LOE B).
During EVT procedure

- Extreme caution should be taken to avoid relative hypotension during the procedure, especially when general anesthesia is used. (BP variability)

- SBP > 140 mm Hg is generally targeted during the procedure, as BP below this threshold has been shown to be independently predictive of poor neurologic outcomes after endovascular treatment. Treurniet er Al; MR CLEAN investigators. A decrease in BP is associated with unfavorable outcome in patients undergoing thrombectomy under general anesthesia. J Neurointerv Surg 2017.
Hyperacute BP management in ICH

- Incidence 10-20/100 000
- ICH mortality: 40-50% in first 30 days
- Consist of 3 phases: - Initial Hematoma
  - Hematoma Expansion
  - Peri-Hematoma Edema

- While earlier studies suggested that aggressive BP lowering in ICH is associated with reduced hematoma growth, larger RCTs showed no advantage to aggressive BP control for most clinical outcomes
70-75% of ICH present with SBP >140.

38% of patients with ICH have a secondary Hematoma expansion (HE) within first 24h.

HE is defined as increased ICH volume by 33% from baseline.

High BP admission and hematoma expansion is associated to worse outcome.

Attempt to prevent or ameliorate hematoma expansion has failed or been limited (small studies).

Driving force of ICH is hydrostatic pressure, BP reduction might be helpful reducing risk HE.
Hematoma Expansion

Stroke 1996;27:1783-87
The risk for early neurologic deterioration and the high rate of poor long term outcomes underscore the need for aggressive early management.

For ICH patients presenting with SBP between 150 and 220 mm Hg and without contraindication to acute BP treatment, acute lowering of SBP to 140 mm Hg is safe Class I; Level of Evidence A, and can be effective for improving functional outcome Class IIa; Level of Evidence B

For ICH patients presenting with systolic BP above 220 mm Hg, it may be reasonable to consider aggressive reduction of BP with continuous intravenous infusion and frequent BP monitoring. Class IIb, LOE C
How low should we go?

- Still a moving target!!
- “The devil is in the details “
- What is the evidence?

Blood Pressure Goals

So what SBP is best to obtain maximal perfusion with the least risk of worsening hemorrhage?

120???
180???
140???
160???
INTERACT II

- N=2794

- Treatment arm: SBP <140
  Control arm: SBP <180

- Patients within 6 hours of onset of ICH

Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D., Candice Delcourt, M.D., Richard Lindley, M.D., Thompson Robinson, M.D., Pablo Lavados, M.D., M.P.H., Bruce Neal, M.D., Ph.D., Jun Hata, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Mark Parsons, M.D., Ph.D., Yuechun Li, M.D., Jinchao Wang, M.D., Stephane Heritier, Ph.D., Qiang Li, B.Sc., Mark Woodward, Ph.D., R. John Simes, M.D., Ph.D., Stephen M. Davis, M.D., and John Chalmers, M.D., Ph.D., for the INTERACT2 Investigators*
OUTCOMES

- No difference between groups in death or major disability at 3 months.

- Ordinal analysis suggested reduced disability in Intensive BP lowering group.

- Recent analysis suggested subgroup with earlier <1h and more pronounced BP reduction had reduced Hematoma expansion in “few mm range”. Carcel C et al. Degree and timing of intensive BP lowering on hematoma in ICH: INTERACT 2 results: Stroke 2016.

- Neutral result explained in part by failure to reach target Value: 1h target SBP in 44%.

- Meta analysis on 7 RCTs on BP lowering in ICH (N=3000) concluded that early BP lowering (SBP<140) is at least well tolerated and feasible with a chance to improve functional outcome. Gioia et Al: Blood pressure management in acute ICH. Curr opin Crit Care 2015;21: 99-106
**ATACH II**

- Aggressive (SBP goal <140) or standard (SBP goal <180) arms with BP control achieved < 4.5 h via nicardipine or, alternatively, via labetalol or diltiazem. Strict control within these parameters was maintained for 24 hours. <1h in 88%.

**Primary Outcome:** Death or disability at 3 months after randomization.

N = 1000 (500 to each group)
- Standard group (SBP 140 – 179 mmHg)
- Intensive group (SBP 110 – 139 mmHg)

**Eligibility:**
- ICH volume < 60 ml
- GCS > 5

**Conclusions:**
- Target SBP 110 – 139 mmHg did not result in lower rate of death or disability compared to the standard treatment group 140 – 179 mmHg.
- Stopped early due to futility and adverse events (ie. renal injury)
ATACH II

- **P:**
  - Patients > 18 years with intracerebral hemorrhage (< 60 cm3) and a GCS ≥5 who presented within 4.5 hours of symptom onset and at least one blood pressure reading with an SBP ≥180 mm Hg
  
- **I:**
  - Aggressively lowering blood pressure to an SBP = 110-139 mmHg for 24 hours using nicardipine (1st line) and labetalol, diltiazem or urapidil (2nd line)
  
- **C:**
  - Standard treatment guided at a SBP = 140 - 179 mm Hg for 24 hours using nicardipine (1st line) and labetalol, diltiazem or urapidil (2nd line)
  
- **O:**
  - Primary: Death or disability [Modified Rankin Scale (mRS) 4-6] at 90 days
  - Secondary: EQ-5D utility index score at 3 months, > 33% expansion of hematoma at 24 hours

### Primary Outcome [Death or disability (mRS 4-6)]

- Standard treatment: 37.7% (181/480)
- Intensive treatment: 38.7% (186/481)
- Relative Risk: 1.02 (95% CI 0.83 – 1.25)
- No statistically significant difference between groups
- Study was stopped early due to futility for the primary outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>RR (95% CI; p Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematoma Expansion</td>
<td>18.9%</td>
<td>24.4%</td>
<td>0.78 (0.49 - 1.04; p = 0.09)</td>
</tr>
<tr>
<td>Neurologic Deterioration within 24Hrs</td>
<td>11.6%</td>
<td>8.0%</td>
<td>1.38 (0.92 - 2.07; p = 0.13)</td>
</tr>
<tr>
<td>Serious Adverse Events within 72Hrs</td>
<td>1.6%</td>
<td>1.2%</td>
<td>1.33 (0.46 - 3.84; p = 0.60)</td>
</tr>
<tr>
<td>Serious Adverse Events within 3 Months</td>
<td>25.6%</td>
<td>20.0%</td>
<td>1.28 (0.99 - 1.66; p = 0.06)</td>
</tr>
<tr>
<td>Renal Adverse Events at 7d</td>
<td>9.0%</td>
<td>4.0%</td>
<td>p = 0.002</td>
</tr>
<tr>
<td>Death</td>
<td>4.6%</td>
<td>6.8%</td>
<td>0.67 (0.46 - 0.97; p = 0.09)</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
<td>12.6</td>
<td>7.0</td>
<td>-1.14 (-2.28 - 0.09; p = 0.05)</td>
</tr>
</tbody>
</table>

“The treatment of participants with intracerebral hemorrhage to achieve a target systolic blood pressure of 110 to 139 mm Hg did not result in a lower rate of death or disability than standard reduction to a target of 140 to 179 mm Hg.”
Significantly more renal adverse events in the intensive BP lowering group

9% vs 4%  p< 0.0002
What did we learn from these 2 Trials?

- Faster BP reduction and more pronounced in ATACH II (120-130 vs 135-145 in INTERACT II) may have been “too much” in degree of BP reduction.

- The lack of effect of intensive BP lowering in reducing Hematoma growth observed in both trials.

- Both trials failed to show efficacy on intensive BP lowering argue against overzealous BP lowering during first few hours after an ICH.

- Despite the guidelines in my practice therefore we lower SBP below 160 especially in known h/o Htn and /or previous renal impairment.
Gap in Knowledge

All BP studies in ICH (small volume 10-15 cc) barely represent the population in the ICU that we see (large volume ICH) so extrapolating those findings to critical care patients is very limited.

The question whether active acute BP lowering can improve outcome remains unanswered.
THANK YOU