Update on treatment of stroke due to intracerebral haemorrhage (ICH)

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MRC senior clinical fellow
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www.RUSH.ed.ac.uk  @BleedingStroke  …/bleedingstroke
My competing interests

Salary

Editorial boards

Research grants

www.whopaysthisdoctor.org
# 15 minutes to tell you about...

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<thead>
<tr>
<th>Recent results</th>
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<tbody>
<tr>
<td><strong>Acute BP lowering</strong></td>
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<tr>
<td><img src="image1.png" alt="Blood Pressure Monitor" /></td>
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<tr>
<td><strong>Acute haemostasis</strong></td>
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<td><img src="image2.png" alt="Blood Vessel" /></td>
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<td><strong>Secondary prevention</strong></td>
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<td><img src="image3.png" alt="Ticagrelor" /></td>
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Acute ↓BP RCTs

<table>
<thead>
<tr>
<th>Open RCT</th>
<th>Year</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERACT-1</td>
<td>2008</td>
<td>404</td>
</tr>
<tr>
<td>Koch et al.</td>
<td>2008</td>
<td>42</td>
</tr>
<tr>
<td>ICH ADAPT</td>
<td>2013</td>
<td>75</td>
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<tr>
<td>INTERACT-2</td>
<td>2013</td>
<td>2,794</td>
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Pooled estimate (RE) 3,315
OR 0.88 (95%CI 0.77-1.01) p=0.07
I² = 0%

Death or dependence at 3m (OR)
Favours intensive  Favours guideline

Neurology 2014;83:1523-9
Distribution of modified Rankin Scale scores at day 90 for patients randomised <6 hours. Adjusted common OR 0.19 (95% CI 0.06 to 0.59, p=0.004)

Lancet 2015;385:617-28

Stroke 2016;47:44-52
Acute ↓BP RCT

Relative risk 1.04 (95%CI 0.85 to 1.27)

**NEJM** June 8, 2016 DOI 10.1056/NEJMoa1603460
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<td><img src="image1" alt="BP Monitor" /></td>
<td><img src="image2" alt="ATACH-II" /> <img src="image3" alt="ENOS" /> <img src="image4" alt="RiIGHT-2" /></td>
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<tr>
<td><strong>Acute haemostasis</strong></td>
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<td><img src="image5" alt="Blood Vessel" /></td>
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Acute platelet transfusion RCT

Inclusion criteria
- Spontaneous supratentorial ICH (no AVM, aneurysm, trauma)
- ≥18 years
- GCS 8-15
- Antiplatelet therapy use for ≥7 days before ICH

Exclusion criteria
- Planned surgery <24h
- Vitamin K antagonist
- Thrombocytopenia
- Transfusion reaction
- mRS ≥2 before ICH
- Death appears imminent

Acute platelet transfusion RCT

190 patients enrolled
190 randomised

97 randomly assigned to platelet transfusion
4 did not receive platelet transfusion
1 refused
1 ineligible
1 died before transfusion
1 transfusion arrived late
93 received platelet transfusion
97 included in intention-to-treat analysis
95 included in as-treated analysis

93 randomly assigned to standard care
2 received platelet transfusion
1 due to deterioration
1 due to misinterpretation of treatment allocation
91 received standard care
93 included in intention-to-treat analysis
95 included in as-treated analysis

Lancet 2016;387:2605-13
Acute platelet transfusion RCT

Adjusted common OR 2.05 (95% CI 1.18 to 3.56), p=0.0114
mRS 4-6, OR 2.04 (95% CI 1.12 to 3.74), p=0.0195

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Anticoagulants after ICH: observational study

Ischaemic stroke, systemic embolism, all cause mortality
Ischaemic stroke or systemic embolism
All cause mortality
Recurrent ICH
Major extracranial bleeding

Adjusted HR over 1 year

Circulation 2015;132:517-25
Anticoagulants after ICH: observational study

JAMA 2015;313:824-36
Later ↓BP after ICH: observational study

JAMA 2015;314:904-12
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<td><img src="image" alt="PATCH" /> <img src="image" alt="TICCH-2" /></td>
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<td><img src="image" alt="RETRACE" /> <img src="image" alt="CAGR" /> <img src="image" alt="TRIDENT" /></td>
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Randomised restart of antiplatelet drugs

On antithrombotics for vaso-occlusive disease prevention + spontaneous ICH

Brain MRI before randomisation (stratification)

Randomisation (central)

1:1

360 START antiplatelet drugs*

360 AVOID antiplatelet drugs

Hospital discharge: serious vascular events (local)

Annual for ≥2yrs: serious vascular events (central via participant &/or GP)

* Aspirin ± clopidogrel ± dipyridamole
Big and simple trial

- Big: 120 sites
- Simple: 4 inclusion criteria
- Easy:
  - Remote training and initiation, research nurse recruitment, prescribing policy, only two forms to complete, minimal AE reporting, central follow-up
Help us if you can!
Peter Langhorne
Professor of Stroke Care, University of Glasgow
“RESTART is important because this kind of clinical question will never be reliably answered by any approach other than a randomised controlled trial”

Keith Muir
SINAPSE Professor of clinical imaging & consultant neurologist, University of Glasgow
“RESTART addresses a scenario for which we lack good quality evidence to guide treatment decisions. Randomising in the trial offers the best opportunity to address an important clinical question”