The acute management of intracerebral haemorrhage

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Intracerebral haemorrhage

- **Common health problem**
  - Causes 10-15% of strokes
  - More common in Asian populations

- **Poor patient outcomes**
  - Case fatality 30-40% at 1 month
  - Causes 5.8% of all global deaths (vs. 6.0% for ischaemic stroke)
  - Only 20% regain independence
  - Little improvement in outcomes over last 30 years

The 10 leading causes of death in the world 2012

- Ischaemic heart disease 7.4m
- Stroke 6.7m
- COPD 3.1m
- Lower respiratory infections 3.1m
- Trachea bronchus lung cancers 1.6m
- HIV / AIDS 1.5m
- Diarrhoeal diseases 1.5m
- Diabetes mellitus 1.5m
- Road injury 1.3m
- Hypertensive heart disease 1.1m
Evidence of nihilism in ICH?

*Adjusted for sex, age, premorbid mRS, comorbidities of congestive heart failure, hypertension, AF, and diabetes, previous stroke/TIA, Level of consciousness, and ‘out of hours’. † also adjusted for early neurological deterioration (drop in NIHSS 1a of 1 or more in first week).

The acute management of intracerebral haemorrhage part 1

Hyperacute management: what to do?
An illustrative case...

- 69 year-old female
- Chronic hypertension, atrial fibrillation
- DH: Perindopril, warfarin (INR target range 2-3)
- Baseline function normal (mRS = 0)
- Sudden onset slurred speech and right-sided weakness at 08:00
- Examination on arrival (09:00):
  - GCS E3 M6 V5 – 14/15
  - Severe R-sided weakness
  - NIHSS 12
  - BP 189/110
CT brain at 09:23 - 1.5 h post-onset
Acute management questions....

1. What should I do about the warfarin treatment?
2. Do I need to do anything about her blood pressure?
3. Should I refer her to the neurosurgeons?
4. Why did she have the intracerebral haemorrhage and do I need to do any further brain scans?
Acute management questions....

1. What should I do about the warfarin treatment?
2. Do I need to do anything about her blood pressure?
3. Should I refer her to the neurosurgeons?
4. Why did she have the intracerebral haemorrhage and do I need to do any further brain scans?
## Anticoagulants – recent Salford audit data

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>No anticoag</td>
<td>32</td>
<td>39</td>
<td>39</td>
<td>39</td>
<td>36</td>
<td>43</td>
<td>59</td>
<td>49</td>
<td>65</td>
<td>72</td>
<td>63</td>
<td>61</td>
<td>28</td>
</tr>
<tr>
<td>VKA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>8</td>
<td>6</td>
<td>11</td>
<td>6</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>DOAC</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>7</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>
VKA-ICH vs. DOAC-ICH

International, multicentre pooled analysis
13 centres – Europe, Asia, North America
500 patients (97 DOAC-ICH; 403 VKA-ICH)

<table>
<thead>
<tr>
<th>Variable</th>
<th>DOAC-ICH (n=97)</th>
<th>VKA-ICH (n=403)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>80 (74-85)</td>
<td>80 (72-85)</td>
</tr>
<tr>
<td>GCS</td>
<td>14 (12-15)</td>
<td>15 (13-15)</td>
</tr>
<tr>
<td>ICH vol</td>
<td>14.4 (3.6-38.4)</td>
<td>10.6 (4.0-27.9)</td>
</tr>
<tr>
<td>IVH</td>
<td>42 (43)</td>
<td>146 (36)</td>
</tr>
<tr>
<td>Pre-mRS</td>
<td>1 (0 to 3)</td>
<td>0 (0 to 2)</td>
</tr>
</tbody>
</table>

Wilson et al, *Neurology*, 2017
VKA-ICH vs. DOAC-ICH

VKA-ICH: INCH trial

- Randomised, open-label, blinded-endpoint trial
- Within 12 h of onset, INR ≥ 2
- 20 mL/kg FFP vs. 30 IU/kg 4F PCC
- 23 FFP & 27 PCC treated

Outcomes:
- INR<1.3 by 3h: 9% FFP vs. 67% PCC
- 90d mortality: 35% FFP vs. 19% PCC
- Increased expansion with FFP
VKA-ICH: ‘Time is brain’

VKA-ICH: Improving door-to-needle times

Three key changes:
1. PCC stock in the ED
2. Point-of-care INR device
3. Standard protocol to deliver PCC without Haematology referral for every case

# DOAC-ICH

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half life</th>
<th>Mode of action</th>
<th>Coagulation tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>12-17 h</td>
<td>Direct thrombin (II)</td>
<td>aPTT, TT</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>7-11 h</td>
<td>Factor Xa</td>
<td>PT, anti Xa</td>
</tr>
<tr>
<td>Apixaban</td>
<td>8-15 h</td>
<td>Factor Xa</td>
<td>anti Xa</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>10-14 h</td>
<td>Factor Xa</td>
<td>PT, anti Xa</td>
</tr>
</tbody>
</table>

Options for reversal:
- PCC (3-factor, 4-factor)
- Idarucizumab (for dabigatran)
- Andexanet alpha (for Xa inhibitors) – *not yet available
DOAC-ICH: current guidelines

What do the guidelines say?

• RCP (2016): idarucizumab for dabigatran; 4F PCC for others
• AHA/ASA (2015): PCC or rFVIIa ‘might be considered’; Activated charcoal might be used if <2 h since last dose; Haemodialysis for dabigatran.
• ESO (2014): No recommendation

PCC:
• Animal and healthy volunteer data suggests partial reversal
• British Committee for Standards in Haematology (2013)
DOAC-ICH: Idarucizumab

- Dabigatran antidote, humanised Fab
- Dabigatran - 350x higher affinity for idarucizumab than thrombin
- Rapid & complete reversal
- No prothrombotic effects in volunteers; 1 in 90 pts (RE-VERSE AD)
- RE-VERSE AD included 18 ICHs
- £2400 per dose (5 g)

Platelet transfusion – for ICH on antiplatelets

- Sometimes used in practice – makes sense?
- PATCH trial: platelet transfusion vs. standard care
  - 190 pts, < 6 h post onset, on antiplatelet drugs

Acute management questions....

1. What should I do about the warfarin treatment?
2. Do I need to do anything about her blood pressure?
3. Should I refer her to the neurosurgeons?
4. Why did she have the intracerebral haemorrhage and do I need to do any further brain scans?
<table>
<thead>
<tr>
<th>Target SBP – intensive group</th>
<th>INTERACT2</th>
<th>ATACH-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 140 mmHg by 1 h stop if &lt; 130 mmHg</td>
<td>110-139 by 2 h</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Target SBP – standard group</th>
<th>INTERACT2</th>
<th>ATACH-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 180 mmHg target 160/90 (AHA 2010)</td>
<td>140-179 by 2 h</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Agents used</th>
<th>INTERACT2</th>
<th>ATACH-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-blocker (urapadil) – 32.5%</td>
<td></td>
<td>First line: nicardipine</td>
</tr>
<tr>
<td>Ca²⁺ channel blocker – 16.2%</td>
<td></td>
<td>Second line:</td>
</tr>
<tr>
<td>Nitroglycerin – 14.9%</td>
<td></td>
<td>Labetolol</td>
</tr>
<tr>
<td>α/β blocker (labetalol) – 14.4%</td>
<td></td>
<td>Urapadil</td>
</tr>
<tr>
<td>Diuretics – 12.4%</td>
<td></td>
<td>Diltiazem</td>
</tr>
<tr>
<td>Nitroprusside 12.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others – 12%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SBP achieved with treatment</th>
<th>INTERACT2</th>
<th>ATACH-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean at 1 h:</td>
<td>150 mmHg (intensive)</td>
<td>129 mmHg (intensive)</td>
</tr>
<tr>
<td></td>
<td>164 mmHg (standard)</td>
<td>141 mmHg (standard)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>mRS 4-6</th>
<th>mRS 4-6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>52.0% (I) vs 55.6% (S) (p=0.06)</td>
<td>38.7% (I) vs. 37.7% (S) (p=0.72)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary outcomes</th>
<th>Ordinal shift: 0.87 (0.77–1.00) p=0.04</th>
<th>Ordinal shift: 1.07 (p=0.56)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EQ5D: 0.60 (I) vs 0.55 (S); p=0.002</td>
<td>EQ5D: 0.7 (I) vs 0.7 (S); p=0.47</td>
</tr>
<tr>
<td></td>
<td>SAEs: 23.3% (I) vs 23.6% (S)</td>
<td>Renal AEs: 9%(I) vs.4%(S) p=0.002</td>
</tr>
</tbody>
</table>

Current UK practice

2016 RCP guideline: recommends INTERACT intervention

Survey of BASP members Feb 2017 (243 respondents):

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there a hyperacute ICH BP protocol in place at centre?</td>
<td>Yes - 69%</td>
</tr>
<tr>
<td>Do you routinely deliver the INTERACT intervention?</td>
<td>Yes - 57%</td>
</tr>
<tr>
<td>If not, why not?</td>
<td></td>
</tr>
<tr>
<td>No locally agreed protocol – 25%</td>
<td></td>
</tr>
<tr>
<td>Not convinced by evidence – 13%</td>
<td></td>
</tr>
<tr>
<td>Not confident can safely deliver – 8%</td>
<td></td>
</tr>
<tr>
<td>Lack resources – 6%</td>
<td></td>
</tr>
<tr>
<td>Preferred first line parenteral drug for BP lowering in ICH?</td>
<td>Labetalol – 56%</td>
</tr>
<tr>
<td></td>
<td>GTN: IV – 23%, transdermal – 15%</td>
</tr>
</tbody>
</table>
Acute management questions....

1. What should I do about the warfarin treatment?
2. Do I need to do anything about her blood pressure?
3. Should I refer her to the neurosurgeons?
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Neurosurgery for ICH

• Infratentorial ICH
  – Risk of brainstem compression, herniation syndromes, hydrocephalus
  – Procedures – EVD / posterior fossa decompression / haematoma evacuation

• Supratentorial ICH – procedures
  – Early haematoma evacuation in the stable patient
  – Haematoma evacuation in the deteriorating patient
  – External ventricular drainage for hydrocephalus
  – External ventricular drainage and clot lysis?
## Early haematoma evacuation in the stable patient

Mendelow et al. (2013) *Lancet* 382:397–408

### Table A

<table>
<thead>
<tr>
<th>Study</th>
<th>Surgery</th>
<th>Control</th>
<th>Peto odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McKissock, et al(^5) (1961)</td>
<td>71/89</td>
<td>60/91</td>
<td>2.00 (1.04-3.86)</td>
</tr>
<tr>
<td>Auer, et al(^1) (1989)</td>
<td>28/50</td>
<td>37/50</td>
<td>0.46 (0.20-1.04)</td>
</tr>
<tr>
<td>Juvela, et al(^4) (1989)</td>
<td>25/26</td>
<td>21/26</td>
<td>4.39 (0.81-23.65)</td>
</tr>
<tr>
<td>Batjer, et al(^3) (1990)</td>
<td>6/8</td>
<td>11/13</td>
<td>0.55 (0.06-4.93)</td>
</tr>
<tr>
<td>Chen, et al(^8) (1992)</td>
<td>40/64</td>
<td>31/62</td>
<td>1.66 (0.82-3.34)</td>
</tr>
<tr>
<td>Morgenstern, et al(^6) (1998)</td>
<td>9/15</td>
<td>11/16</td>
<td>0.69 (0.16-2.94)</td>
</tr>
<tr>
<td>Zuccarello, et al(^7) (1999)</td>
<td>4/9</td>
<td>7/11</td>
<td>0.48 (0.09-2.69)</td>
</tr>
<tr>
<td>Chen, et al(^3) (2001)</td>
<td>86/263</td>
<td>97/230</td>
<td>0.67 (0.46-0.96)</td>
</tr>
<tr>
<td>Teemstra, et al(^9) (2001)</td>
<td>33/36</td>
<td>29/33</td>
<td>1.51 (0.32-7.12)</td>
</tr>
<tr>
<td>Hosseini, et al(^2) (2003)</td>
<td>0/1</td>
<td>0/1</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Hattori, et al(^3) (2004)</td>
<td>60/121</td>
<td>82/121</td>
<td>0.47 (0.28-0.79)</td>
</tr>
<tr>
<td>Mendelow, et al(^10) (2005)</td>
<td>346/468</td>
<td>378/496</td>
<td>0.89 (0.66-1.19)</td>
</tr>
<tr>
<td>Pantazis, et al(^4) (2006)</td>
<td>36/54</td>
<td>49/54</td>
<td>0.24 (0.10-0.60)</td>
</tr>
<tr>
<td>Wang, et al(^5) (2009)</td>
<td>87/194</td>
<td>120/181</td>
<td>0.42 (0.28-0.63)</td>
</tr>
<tr>
<td>Mendelow, et al (2013)</td>
<td>174/297</td>
<td>178/286</td>
<td>0.86 (0.62-1.20)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1695</td>
<td>1671</td>
<td>0.74 (0.64-0.86)</td>
</tr>
</tbody>
</table>

Total events: 1005 (surgery), 1111 (control)
Test for heterogeneity: \( \chi^2 = 39.29, df = 13 \) (p=0.0002), I\(^2\) = 66.9%
Test for overall effect: Z=4.00 (p<0.0001)

**Minimally invasive surgery**
Early haematoma evacuation

- IPD meta-analysis – 2186 cases
- Overall benefit in cases:
  - Onset to randomisation < 8h
  - Age 50-70
  - GCS 9-12
  - ICH volume 20-50 ml

Gregson et al. (2012) Stroke 43: 1496-1504
**MISTIE III: MIS and tPA for ICH**

- Catheter *in situ* from 1-2 days post onset, for 3-6 days
- tPA administered in to haematoma via catheter every 8 h
- **Phase II trial:**
  - 96 patients (54 surgery, 42 conservative)
  - 180d mRS $\leq 3$: 21% cons vs. 33% MIS (adjusted for p=0.049)

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Aetiology of ICH

**STRUCTURAL**
- Hypertensive microangiopathy
- Cerebral amyloid angiopathy
- Neoplasm (primary/metastasis)
- Haemorrhagic transformation of cerebral infarction
- Intracranial vascular malformation
- Intracranial arterial aneurysm
- Intracranial venous thrombosis
- Dural arteriovenous fistula
- Septic arteritis / vasculitis

**HAEMOSTATIC/HAEMODYNAMIC**
- Hypertension
- Anticoagulation
- Thrombolytic treatment
- Antiplatelets
- Clotting factor deficiency
- Thrombocytopenia
Further investigation

• **Aim:** Identify causes needing specific treatment
  1. Vascular malformations – surgery / endovascular / radiosurgery
  2. Tumours – surgery / radiotherapy / chemotherapy
  3. CVST – anticoagulation
  4. Endocarditis - antibiotics

• **Options:**
  - CT angiography – readily available at most centres
  - MRI/MRA – detailed assessment of brain parenchyma, evidence for CAA (microbleeds, siderosis, enlarged PVS)
  - Catheter angiography - high sensitivity for vascular malformations, but risk of complications
The acute management of intracerebral haemorrhage part 2

Hyperacute management: how to do it?
Acute Bundle of Care for ICH (ABC-ICH) project

**Design:** Single centre quality improvement project and evaluation

**Site:** Salford Royal Hospital, Greater Manchester, UK

**Aim:** 10 percentage point reduction in 30-day case fatality after admission with acute ICH by the end of 2016.

**Methods:**

- Model for Improvement used to conduct QI project
- Improvement phase: June 2015 – June 2016
- Data entered in QI registry from Jun 2013 – Jan 2017
- All spontaneous ICH included (excluded traumatic ICH, haemorrhagic transformation)
**Aim:** By Dec 2016, 10 percentage point reduction in 30-day case fatality after admission to Salford with acute ICH

- **Anticoagulants:** Recognition as emergency, Fast reversal
- **Blood pressure:** Intensive BP lowering, Early enteral treatment
- **Neurosurgery:** Timely, focused referrals, ICH MDT meetings
- **Supportive care:** Improved access to critical care, Reduction in DNR orders
The ABC hyperacute care bundle

A. Anticoagulant reversal: Deliver reversal agent < 90 min from arrival

B. Blood pressure lowering: Deliver intensive blood pressure lowering with needle-to-target time < 60 min

C. Care pathway: Refer patients with good pre-morbid function (mRS ≤ 2) and any of the following to Neurosurgery:
   - GCS < 9
   - Posterior fossa ICH
   - Obstructed 3\textsuperscript{rd}/4\textsuperscript{th} ventricle
   - Haematoma volume > 30 ml
Anticoagulant reversal – DNT by quarter

DNT (min)

Target = 90 min

Pre QI

Post QI

2013-Q2
2013-Q3
2013-Q4
2014-Q1
2014-Q2
2014-Q3
2014-Q4
2015-Q1
2015-Q2
2015-Q3
2015-Q4
2016-Q1
2016-Q2
2016-Q3
2016-Q4
2017-Q1

↑ POC INR

↑ Education and awareness work
Intensive BP lowering – NTT by month

INTERACT2 published
Protocol introduced
Change to GTN first
Neurosurgery - operations per quarter

operations / quarter

Pre Q1 | Post Q1

Critical care admissions - % by quarter

Percent

Pre QI | Post QI


0% | 5% | 10% | 15% | 20% | 25% | 30% | 35% | 40% |
Baseline characteristics

<table>
<thead>
<tr>
<th>Factor</th>
<th>Pre QI (n=381)</th>
<th>Post QI (n=449)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>71.8 (57.0 – 81.2)</td>
<td>70.6 (56.8 – 80.3)</td>
<td>0.96</td>
</tr>
<tr>
<td>Premorbid mRS (0-2)</td>
<td>305 (80.1%)</td>
<td>370 (82.4%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>55 (14.4%)</td>
<td>57 (12.7%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>199 (52.2%)</td>
<td>232 (51.7%)</td>
<td>0.89</td>
</tr>
<tr>
<td>GCS</td>
<td>14 (10-15)</td>
<td>14 (11-15)</td>
<td>0.94</td>
</tr>
<tr>
<td>Infratentorial</td>
<td>45 (11.8%)</td>
<td>55 (12.2%)</td>
<td>0.92</td>
</tr>
<tr>
<td>IVH</td>
<td>147 (38.7%)</td>
<td>168 (37.4%)</td>
<td>0.72</td>
</tr>
<tr>
<td>ICH volume (ml)</td>
<td>19.0 (6.4 – 51.7)</td>
<td>17.1 (5.1 – 44.8)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Kaplan-Meier analysis

Pre-QI project commencement:
• Jul 2013 – May 2015
• 381 cases admitted
• 30-day case fatality = 33.9%

Post-QI project commencement:
• Jun 2015 – Jul 2016
• 449 cases admitted
• 30-day case fatality = 23.4%

Logrank test: \( p=0.001 \)
## Cox regression analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>HR</th>
<th>95% CI</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS</td>
<td>0.87</td>
<td>0.84 to 0.89</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>1.38</td>
<td>1.06 to 1.81</td>
<td>0.018</td>
</tr>
<tr>
<td>Infratentorial</td>
<td>1.78</td>
<td>1.32 to 2.39</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IVH</td>
<td>1.38</td>
<td>1.11 to 1.73</td>
<td>0.05</td>
</tr>
<tr>
<td>ICH vol</td>
<td>1.007</td>
<td>1.005 to 1.009</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age</td>
<td>1.053</td>
<td>1.043 to 1.063</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Post QI</strong></td>
<td><strong>0.67</strong></td>
<td><strong>0.54 to 0.84</strong></td>
<td><strong>&lt;0.0001</strong></td>
</tr>
<tr>
<td>Post QI (unadj)</td>
<td>0.69</td>
<td>0.55 to 0.86</td>
<td>0.001</td>
</tr>
</tbody>
</table>
ABC-ICH: GM scale-up

Aim: A 10% reduction in death and severe disability (mRS 4-6) after acute ICH by April 2018 in Greater Manchester

Implementation:
• Launch bundle at Stepping Hill and Fairfield from Apr 2017
• Greater Manchester care pathway introduced April 2017

Measurement:
• App/EPR tools for acute team linked to dashboard of key measures
• Collection of mRS (disability scale) at 6 month
Greater Manchester ICH care pathway

**GCS ≤ 8**
1. Stabilise
2. Reverse anticoagulation
3. Refer to neurosurgery if mRS < 3
4. Discuss with HASU (if not accepted by NS)

**GCS ≥ 9**
1. Reverse anticoagulation
2. Blood pressure lowering (at HASU only)
3. Refer to neurosurgery if mRS < 3 and:
   - Post fossa, or
   - Obstructed 3\textsuperscript{rd}/4\textsuperscript{th} ventricle, or
   - Haematoma volume > 30 ml, or
   - GCS 9-12
4. Transfer to HASU if < 48 h post-onset

http://gmsodn.org.uk – Intracerebral Haemorrhage Pathway section
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http://gmsodn.org.uk – Intracerebral Haemorrhage Pathway section
Neurosurgical criteria – retrospective analysis

799 ICHs in registry (Jun 13 – Oct 16)

776 ICHs with pre-morbid mRS

625 mRS 0-2

507 mRS 0-2 GCS ≥ 9

452 mRS 0-2 supratent No obst

425 mRS 0-2 supratent

309 no referral 8 surgery (2.6%)

23 missing pre-morbid mRS

151 mRS 3-5 2 had surgery (1.3%)

118 cases with GCS ≤ 8 54 had surgery (45.8%)

36 cerebellar 10 had surgery (27.8%)

19 brainstem 0 had surgery

116 vol ≥ 30ml 25 had surgery (21.6%)
Operations not meeting criteria

**mRS ≥ 3 (2 cases, 0.3% of all cases)**
- mRS 3, 78, obstructive hydrocephalus, R cerebellar, EVD at day 2, died day 6
- mRS 4, 51, learning difficulties, obstructive hydrocephalus, EVD, died day 10

**mRS 0-2, no indication (0.6% of all cases)**
- 1 case with surgery in first 7 days due to HE
- 2 surgery > 1 week later for delayed hydrocephalus
- 2 for biopsy of lesion semi-electively
- 3 in MISTIE