Hyperacute and Acute Stroke Care: What’s New?

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What’s new in hyperacute and acute care

- Mechanical thrombectomy (MT)
- IV Thrombolysis (IVT)
- Acute BP lowering
- Acute imaging
- Stroke unit care

National clinical guideline for stroke
Prepared by the Intercollegiate Stroke Working Party
Fifth Edition 2016
Thrombectomy: the game changer

Stent retriever (Solitaire)
The primary efficacy studies

- MR CLEAN
- EXTEND-IA
- ESCAPE
- REVASCAT
- SWIFT-PRIME
- THRACE
- THERAPY
- PISTE
- Individual patient meta-analysis: HERMES
**A Overall**

- **Control population (n=645)**
  - 5.0 7.9 13.6 16.4 24.7 13.5 18.9

- **Intervention population (n=633)**
  - 10.0 16.9 19.1 16.9 15.6 6.2 15.3

**B Ineligible for alteplase**

- **Control population (n=80)**
  - 3.6 6.2 12.5 8.7 31.2 15.0 22.5

- **Intervention population (n=108)**
  - 10.2 15.7 17.6 18.5 7.4 7.4 23.1

**Received alteplase**

- **Control population (n=565)**
  - 5.1 8.1 13.8 17.5 23.7 13.3 18.4

- **Intervention population (n=525)**
  - 9.9 17.1 19.4 16.6 17.3 5.9 13.7

**NNT for a very good outcome (mRS 0-2) = 3.2-7.4**

**NNT for one-better mRS score at 90 days = 2.6**
Time to treatment effect in MR CLEAN

B Effect of time on achieving mRS score of 0-2: all participants

$P = .04$ for interaction

Fransen et al, *JAMA* 2016
ICER = $3110/QALY

Cost-effectiveness of endovascular stroke therapy
Kunz et al
Stroke, November 2016
What does the new guideline say?

G Patients with acute ischaemic stroke should be considered for combination intravenous thrombolysis and intra-arterial clot extraction (using stent retriever and/or aspiration techniques) if they have a proximal intracranial large vessel occlusion causing a disabling neurological deficit (National Institutes of Health Stroke Scale [NIHSS] score of 6 or more) and the procedure can begin (arterial puncture) within 5 hours of known onset.

H Patients with acute ischaemic stroke and a contraindication to intravenous thrombolysis but not to thrombectomy should be considered for intra-arterial clot extraction (using stent retriever and/or aspiration techniques) if they have a proximal intracranial large vessel occlusion causing a disabling neurological deficit (National Institutes of Health Stroke Scale [NIHSS] score of 6 or more) and the procedure can begin (arterial puncture) within 5 hours of known onset.

I Patients with acute ischaemic stroke causing a disabling neurological deficit (a National Institutes of Health Stroke Scale [NIHSS] score of 6 or more) may be considered for intra-arterial clot extraction (using stent retriever and/or aspiration techniques, with prior intravenous thrombolysis unless contraindicated) beyond an onset-to-arterial puncture time of 5 hours if:

- the large artery occlusion is in the posterior circulation, in which case treatment up to 24 hours after onset may be appropriate;
- a favourable profile on salvageable brain tissue imaging has been proven, in which case treatment up to 12 hours after onset may be appropriate.
- No new RCT primary efficacy evidence since IST-3 and the 2012 Cochrane review
- ENCHANTED-dose arm reported lower risk with lower dose, without quite meeting non-inferiority threshold (Anderson et al, 2016)
- Risk factors for intracerebral haemorrhage with IV thrombolysis: AF, CCF, CKD, antiplatelet treatment, leucoaraiosis, visible acute infarction (Whiteley et al, 2012)
Any evidence of a ‘Shinton effect’?

Thrombolysis rate (All stroke)

MHRA report

Source: SSNAP 2013-2016
Team-centred results for Key Indicator 3.1B
National results
What does the new guideline say?

3.5.1 Recommendations

A Patients with acute ischaemic stroke, regardless of age or stroke severity, in whom treatment can be started within 3 hours of known onset should be considered for treatment with alteplase.

B Patients with acute ischaemic stroke under the age of 80 years in whom treatment can be started between 3 and 4.5 hours of known onset should be considered for treatment with alteplase.

C Patients with acute ischaemic stroke over 80 years in whom treatment can be started between 3 and 4.5 hours of known onset should be considered for treatment with alteplase on an individual basis. In doing so, treating clinicians should recognise that the benefits of treatment are smaller than if treated earlier, but that the risks of a worse outcome, including death, will on average not be increased.

The Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANCED) of lower (0.6 mg/kg) versus standard dose alteplase showed a lower risk of intracerebral haemorrhage and early mortality with the lower dose, without conclusively demonstrating that the doses were of equivalent efficacy (Anderson et al, 2016). These findings suggest that there may be circumstances in which the treating physician and/or the patient wish to forgo some of the potential disability benefit from standard dose alteplase in order to reduce the early risk of intracerebral haemorrhage through the use of the lower dose.
What else about IVT?

- Emphasis on expediting pre-hospital assessment, pre-alert and in-hospital processes to maximise benefit

<table>
<thead>
<tr>
<th>Onset-to-Treatment time</th>
<th>Number Needed to Treat to yield one additional patient with minimal disability (mRS 0-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-90 mins</td>
<td>![Icon for 0-90 mins]</td>
</tr>
<tr>
<td>91-180 mins</td>
<td>![Icon for 91-180 mins]</td>
</tr>
<tr>
<td>181-270 mins</td>
<td>![Icon for 181-270 mins]</td>
</tr>
</tbody>
</table>
IVT: speeding up by 2 min 20 secs per year

Door-to-needle

Source: SSNAP 2013-2016
National results for Key Indicator 3.5A

National results
What does the new guideline say?

C. The pre-hospital care of people with suspected stroke should minimise time from call to arrival at hospital and should include a hospital pre-alert to expedite specialist assessment and treatment.

3.4.1 Recommendations

A. Patients with suspected acute stroke should be admitted directly to a hyperacute stroke unit and be assessed for emergency stroke treatments by a specialist physician without delay.

National clinical

E. Alteplase should only be administered within a well-organised stroke service with:
   – processes throughout the emergency pathway to minimise delays to treatment, to ensure that thrombolysis is administered as soon as possible after stroke onset;
Acute BP lowering in ICH

• Two apparently contradictory trials
  — INTERACT-2 (Anderson et al, NEJM 2013): 2839 patients (majority Chinese) within 6 hrs with mainly small, deep ICH; BP target <140 within 1 hr
  — ATACH-2 (Qureshi et al, NEJM 2016): 1000 patients within 4.5 hrs with small, deep ICH; Target 110-139 within 2 hours

• Significant differences between the trials will make meta-analysis difficult
Reconciling INTERACT2 and ATACH2

• Most ATACH-2 patients had BP lowering before randomisation, such that the ‘usual care’ BP in ATACH-2 was similar to the ‘intensive treatment’ BP in INTERACT-2

• INTERACT-2 suggests that BP lowering to that level (SBP=140 mmHg) is likely to be helpful

• ATACH-2 suggests that BP lowering beyond that level is unlikely to help further

• At present, no proven treatment available for ICH other than stroke unit care
What does the new guideline say?

D Patients with primary intracerebral haemorrhage who present within 6 hours of onset with a systolic blood pressure above 150mmHg should be treated urgently using a locally agreed protocol for blood pressure lowering to a systolic blood pressure of 140 mmHg for at least 7 days, unless:
   - the Glasgow Coma Scale score is 5 or less;
   - the haematoma is very large and death is expected;
   - a structural cause for the haematoma is identified;
   - immediate surgery to evacuate the haematoma is planned.

E Patients with intracerebral haemorrhage should be admitted directly to a hyperacute stroke unit for monitoring of conscious level and referred immediately for repeat brain imaging if deterioration occurs.

F Patients with intracranial haemorrhage who develop hydrocephalus should be considered for surgical intervention such as insertion of an external ventricular drain.
Acute brain imaging

- IV Thrombolysis
- Identification of large vessel occlusion prior to thrombectomy (≤40% of acute presentations)
- Acute BP intervention for haemorrhage
- 63% of patients now present within 3 hours of onset
- Cost-effectiveness of acute imaging known since 2004 even without these treatment advances (Wardlaw, *HTA* 2004)
- ‘Incremental approach’ since the 2004 edition
2012 recommendation: all strokes scanned within 12 hours

Scan within 12 hours

Source: SSNAP 2013-2016
Team-centred results for Key Indicator 1.2B
National results
What does the new guideline say?

3.4.1 Recommendations

A  Patients with suspected acute stroke should be admitted directly to a hyperacute stroke unit and be assessed for emergency stroke treatments by a specialist physician without delay.

B  Patients with suspected acute stroke should receive brain imaging urgently and at most within 1 hour of arrival at hospital.

C  Interpretation of acute stroke imaging for thrombolysis decisions should only be made by healthcare professionals who have received appropriate training.

D  Patients with ischaemic stroke who are eligible for endovascular therapy should have a CT angiogram from aortic arch to skull vertex immediately. This should not delay the administration of intravenous thrombolysis.

E  MRI with stroke-specific sequences (diffusion-weighted imaging, T2*) should be performed in patients with suspected acute stroke when there is diagnostic uncertainty.
2016 recommendation: all suspected acute strokes within 1 hour
What are your chances of getting admitted to a stroke unit within 4 hours?

84%

22%

206 out of 211 CCGs (5 removed due to small numbers)

NHS Atlas of Variation 2015
Adjusted hazard ratio of 30 day mortality of patients admitted on a weekday, by ratio of registered nurses per 10 beds on the weekend.

Hazard ratios adjusted for patient casemix, organisational characteristics, staffing and care quality.

Bray et al, PLoS Medicine, 2014
Does it matter how quickly your swallow is screened?

Risk of pneumonia by time to swallow screening for 80,000 patients in SSNAP

Bray et al, the SSNAP Collaboration, *JNNP* 2016
## Hyperacute and acute stroke units

### Table 2.1 Recommended staffing levels for stroke units

<table>
<thead>
<tr>
<th></th>
<th>Physiotherapist</th>
<th>Occupational therapist</th>
<th>Speech and language therapist</th>
<th>Clinical neuropsychologist/clinical psychologist</th>
<th>Dietitian</th>
<th>Nurse</th>
<th>Consultant stroke physician</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-time equivalent (WTE) per 5 beds</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hyperacute Stroke Unit</strong></td>
<td>0.73</td>
<td>0.68</td>
<td>0.34</td>
<td>0.20</td>
<td>0.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acute Stroke Unit</strong></td>
<td>0.84</td>
<td>0.81</td>
<td>0.40</td>
<td>0.20</td>
<td>0.15</td>
<td></td>
<td>24/7 availability; minimum 6 thrombolysis trained physicians on rota</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>1.35</td>
<td>(65:35 registered: unregistered)</td>
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<tr>
<td></td>
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<td></td>
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<td>Consultant-led ward round 5 days/week</td>
</tr>
</tbody>
</table>

WTE per bed

Nurse

Consultant stroke physician

Royal College of Physicians

Sentinel Stroke National Audit Programme (SSNAP)
What does the new guideline say?

2.4.1 Recommendations
A People with stroke should be treated on a specialist stroke unit throughout their hospital stay unless their stroke is not the predominant clinical problem.

3.4.1 Recommendations
A Patients with suspected acute stroke should be admitted directly to a hyperacute stroke unit and be assessed for emergency stroke treatments by a specialist physician without delay.

3.10.1 Recommendations
A Patients with acute stroke should be admitted directly to a hyperacute stroke unit with protocols to maintain normal physiological status and staff trained in their use.

F Until a safe swallowing method is established, patients with dysphagia after acute stroke should:
- be immediately considered for alternative fluids;
- have a comprehensive specialist assessment of their swallowing;
- be considered for nasogastric tube feeding within 24 hours;
- be referred to a dietitian for specialist nutritional assessment, advice and monitoring;
- receive adequate hydration, nutrition and medication by alternative means.
## 10 Clinical Standards for 7-day services

<table>
<thead>
<tr>
<th>Clinical Standard</th>
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<tbody>
<tr>
<td>1. Patients are supported in shared decision-making 7 days a week, supported by high quality information about emergencies</td>
</tr>
<tr>
<td>2. Emergencies with a mortality &gt;10% are assessed and treated by a suitable consultant within an hour (others within 6-14 hrs)</td>
</tr>
<tr>
<td>3. All emergencies must be assessed for complex and on-going needs by the MDT (nursing, medicine, pharmacy, PT and OT) within 14 hrs</td>
</tr>
<tr>
<td>4. Handovers must be standardised over 7 days, and kept to ≤2/day</td>
</tr>
<tr>
<td>5. Consultant-directed diagnostic tests where the test will alter management at the time must be available and reported within 1 hr</td>
</tr>
</tbody>
</table>
## 10 Clinical Standards for 7-day services

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<tr>
<td>6. In-patients have 24/7 access to consultant-directed interventions that meet the relevant specialty guidelines</td>
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<tr>
<td>7. 24/7 access to psychiatric liaison for mental health needs within 14 hours (1 hour for emergencies)</td>
</tr>
<tr>
<td>8. All patients in high-dependency areas must be reviewed by a consultant twice daily. Consultants should work 2-4 day blocks</td>
</tr>
<tr>
<td>9. Support services in hospital and community care must be available 7 days a week</td>
</tr>
<tr>
<td>10. All those involved in patient care must review patient outcomes to drive quality improvement</td>
</tr>
</tbody>
</table>

**Implemented by all acutely admitting stroke centres by autumn 2017**