Intravenous stroke thrombolysis program using telemedicine: outcome and safety

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Background
Mechanism of IV stroke thrombolysis

- **Ischaemic stroke in hyperacute phase**
  - Acute arterial occlusion led to irreversible infarct core with surrounding ischaemic tissues (ischaemic penumbra)
  - Tissue within ischaemic penumbra can be salvaged if blood supply can be restored within the therapeutic window from symptoms onset

- **Infusion of fibrinolytic agent in hyperacute phase**
  - Dissolve the blood clot and recanalize the vessel
  - Lead to recovery of the neurological impairment
Intravenous Thrombolysis

- **NINDS t-PA Stroke Trial**
  - Published in 1995
  - *Within 3 hrs* of stroke onset
    - 58% within 90 min
  - *0.9 mg/kg* iv over 1 hr, *10% of total dose* as bolus, max 90mg
  - US FDA approved 1996
Intravenous Thrombolysis

- More likely to have excellent functional outcome at 3 months (31% to 50% vs. 20% to 38%, absolute difference 11 to 13%)

- Benefit maintained at 1 year

- Cost-effective
  - Discharge earlier to home
  - Less nursing home
  - Less extensive rehabilitation

Outcomes of SITS-MOST compared to randomised controlled trials

<table>
<thead>
<tr>
<th>Outcome</th>
<th>SITS-MOST (events/total; 95% CI)</th>
<th>Pooled RCTs* (events/total; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SICH per NINDS definition†</td>
<td>7.3% (468/6438; 6.7–7.9)</td>
<td>8.6% (40/465; 6.3–11.6)</td>
</tr>
<tr>
<td>Mortality within 3 months</td>
<td>11.3% (701/6218; 10.5–12.1)</td>
<td>17.3% (83/479; 14.1–21.1)</td>
</tr>
<tr>
<td>Independence (mRS 0–2) at 3 months</td>
<td>54.8% (3362/6136; 53.5–56.0)</td>
<td>50.1% (233/465; 44.5–54.7)</td>
</tr>
</tbody>
</table>

Proportions of patients with symptomatic intracerebral haemorrhage, including fatalities, and mortality and independence at 3 months in SITS-MOST and pooled randomised controlled trials.

SICH=symptomatic intracerebral haemorrhage.

*SActive arms. †NIHSS≥1 and any haemorrhage.

IV Thrombolysis in Acute Ischaemic Stroke

• IV thrombolysis is evidence-based
  • NINDS trial as landmark study
  • Meta-analysis of NINDS trial, ECASS I, ECASS II, ATLANTIS suggested the 4.5 hr treatment window
  • ECASS III confirmed the treatment efficacy up to 4.5 hr from symptom onset
  • IST III reinforce the efficacy in elderly patients

• Effectiveness of IV thrombolysis is reproduced outside clinical trial setting
  • STARS (USA, n=389, 97-98)
  • CASES (Canada, n=1135, 99-01)
  • SITS-MOST (Europe, n=6483, 02-06)
  • SITS-ISTR (International, n=23942, 02-08)
Difficulties of Stroke Thrombolysis

- Significant risk of ICH after thrombolysis
- Treatment response is time dependent
- No objective diagnostic investigation in early phase of ischaemic stroke
Safety Concern – Intracranial Hemorrhage

3 Months Outcome by Treatment in NINDS

Mortality rate in both treatment groups was similar at 3 months & at 1 year.

NEJM 1995;333:1581-1587
Treatment Efficacy is Time Dependent

Treatment response is time dependent! Earlier the treatment, Better chance for favourable outcome!
NIH-recommended Emergency Department response times

The “golden hour” for evaluating and treating acute stroke

**door-to-needle ≤60 min**

- **Suspected stroke patient arrives at ED**
- **≤10 min** Initial MD evaluation (including patient history, lab work initiation, and NIH Stroke Scale assessment)
- **≤15 min** Stroke team notified (including neurologic expertise)
- **≤25 min** CT scan initiated
- **≤45 min** CT & labs interpreted
- **≤60 min** Activase® (Alteplase, t-PA) given if patient is eligible

Service Requirement

• Coordinated rapid response

• Neurology expertise needed to select the patient according to clinical and CT criteria
Low Utilization Rate

• Stroke thrombolysis is under-utilized
• Less than 5% of patients was treated

• It is related to:
  • Delayed presentation to A&E
  • Lack of neurologist expertise on site to support the stroke thrombolysis service
Telemedicine for Stroke Thrombolysis
Telestroke

• Application of telemedicine in stroke care
  • Remote evaluation of stroke patient by videoconferencing or telephone consultation
  • Remote review of neuroimaging

• Advantages
  • Overcome the lack of onsite stroke expertise
  • Increase stroke thrombolysis rate
  • Reduce the need of patient transfer

• Outcome similar as compared with treatment with neurologist on site
Telestroke-Guided Intravenous Tissue-type Plasminogen Activator Treatment Achieves a Similar Clinical Outcome as Thrombolysis at a Comprehensive Stroke Center

*Stroke. 2011 Nov;42(11):3291-3*

<table>
<thead>
<tr>
<th></th>
<th>Stroke Centre</th>
<th>Telestroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>59</td>
<td>83</td>
</tr>
<tr>
<td>Age</td>
<td>71.9</td>
<td>71.9</td>
</tr>
<tr>
<td>Median NIHSS</td>
<td>10.5</td>
<td>12</td>
</tr>
<tr>
<td>Door to Needle time</td>
<td>67.8</td>
<td>89.9 (p&lt;0.05)</td>
</tr>
<tr>
<td>Onset to Needle time</td>
<td>156.7</td>
<td>145.5</td>
</tr>
<tr>
<td>sICH (%)</td>
<td>5.1</td>
<td>1.2</td>
</tr>
<tr>
<td>mRS 0-1 (%)</td>
<td>22.0</td>
<td>34.9</td>
</tr>
<tr>
<td>mRS 0-2 (%)</td>
<td>37.5</td>
<td>42.1</td>
</tr>
</tbody>
</table>

**Conclusion:** Telestroke is a viable alternative to in-person evaluation.
Two years of Finnish Telestroke
Thrombolysis at spokes equal to that at the hub

Neurology. 2011;76:11:1145-1152

<table>
<thead>
<tr>
<th></th>
<th>Onsite at HUCH</th>
<th>Finnish telestroke</th>
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<tbody>
<tr>
<td>Number</td>
<td>985</td>
<td>61</td>
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<tr>
<td>Age</td>
<td>67.7</td>
<td>70</td>
</tr>
<tr>
<td>Median NIHSS</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Onset to Needle time</td>
<td>116</td>
<td>130</td>
</tr>
<tr>
<td>sICH (%)</td>
<td>9.4</td>
<td>6.7</td>
</tr>
<tr>
<td>mRS 0-1 (%)</td>
<td>36.8</td>
<td>29.4</td>
</tr>
<tr>
<td>mRS 0-2 (%)</td>
<td>58.1</td>
<td>49.1</td>
</tr>
</tbody>
</table>

**Conclusion:** Outcome of stroke thrombolysis via Finnish Telestroke was very similar to on-site thrombolysis at HUCH.
Development of 24 hr IV Stroke Thrombolysis in Queen Elizabeth Hospital, Hong Kong
IV Stroke Thrombolysis Service in QEH

- Office-hour thrombolysis service started in 2005
  - 2 to 4 patients treated per year
  - Lack of awareness of the service
  - Under identification of eligible patients

- IT development within HA
  - Remote access of patient information (clinical notes, investigation and imaging)
  - Teleradiology is technically feasible

- 24 hour iv stroke thrombolysis service was implemented on Dec 2008, and it is the first 24-hour program in HA
Multi-disciplinary Team

24hr IV rTPA Program

- Neurologist
- Stroke nurse
- A&E Specialist
- ICU
- General Internist
- Neursosurgeon
- Radiologist
Utilization of Teleradiology

Token for remote access of HA ePR and images

Remote access of CT images via computers outside HA system
24hr Services by Internists and Neurologists supported by Telemedicine

Office Hour Or Outside office hours with Neurologist on site

- Assessed and managed by neurologist

Outside office hours without neurologist on site

- Assessed and managed by onsite internist
- Telephone consultation to on call off site Neurologists who will review the CT scan via tele-radiology and make the decision to treat or not
- Informed consent process and treatment initiated by internist

Post Treatment Monitoring

- Admitted to Acute Stroke Unit or ICU for close monitoring
Key Role of Internal Medicine Specialist

✓ Assessment of potentially eligible patients: confirmation of diagnosis, onset time, assessment of stroke severity

✓ Check for any contraindication for iv thrombolysis

✓ Preliminary review of CT scan images

✓ Telephone consultation to on-call neurologist

✓ Clarify the risk/benefit of treatment to patients/relatives (Informed consent)
**QEH Model of Tele-stroke**

- **Telephone-based consultation**
  - Reconfirm onset time
  - Assess stroke severity & bleeding risk
  - Look for contraindication
  - Decision to treat or not

- **Teleradiology**
  - Remote review of CT image via internet access of the hospital image server
  - Guided by ASPECT score
Protocol-driven Management

- Protocol driven with checklist, assessment form, standard treatment order form, patient information sheet & management protocol
- To speed up the screening process
- To standardize the management
Outcome
Neurologist on site vs Internist with telephone consultation and teleradiology
### Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>On site (N=102)</th>
<th>Telemedicine (N=50)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (median)</strong></td>
<td>70.5</td>
<td>65.0</td>
<td>0.234</td>
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<tr>
<td><strong>HT</strong></td>
<td>54.9%</td>
<td>62.0%</td>
<td>0.406</td>
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<tr>
<td><strong>DM</strong></td>
<td>25.5%</td>
<td>18.0%</td>
<td>0.303</td>
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<td><strong>AF</strong></td>
<td>24.5%</td>
<td>24.0%</td>
<td>0.945</td>
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<tr>
<td><strong>Baseline NIHSS</strong></td>
<td>12</td>
<td>12.5</td>
<td>0.843</td>
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<tr>
<td><strong>ASPECT score</strong></td>
<td>10</td>
<td>10</td>
<td>0.882</td>
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## Logistics (Onsite vs. Telemedicine)

<table>
<thead>
<tr>
<th>Median (in minutes)</th>
<th>On site (N=102)</th>
<th>Telemedicine (N=50)</th>
<th>p value</th>
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<tr>
<td>Onset to Door time</td>
<td>54</td>
<td>43.5</td>
<td>0.015</td>
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<td>Door to CT time</td>
<td>26</td>
<td>30</td>
<td>0.291</td>
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<tr>
<td>CT time to Needle time</td>
<td>40.5</td>
<td>67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Door to Needle time</td>
<td>71</td>
<td>96.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Onset to Needle time</td>
<td>133</td>
<td>147.5</td>
<td>0.012</td>
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</table>
## Outcome (Onsite vs. Telemedicine)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>On site (N=102)</th>
<th>Telemedicine (N=50)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Symptomatic ICH</td>
<td>4.9%</td>
<td>4.0%</td>
<td>1.0</td>
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<tr>
<td>mRS 0-1 (3 months)</td>
<td>43.0%</td>
<td>52.1%</td>
<td>0.299</td>
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<tr>
<td>mRS 0-2 (3 months)</td>
<td>54.0%</td>
<td>58.3%</td>
<td>0.620</td>
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<tr>
<td>Mortality (3 months)</td>
<td>11.9%</td>
<td>8.2%</td>
<td>0.583</td>
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</table>
Three Month Functional Outcome

### Bar Graph

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Window</th>
<th>NIHSS Median</th>
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<tbody>
<tr>
<td>ECASS III</td>
<td>3 – 4.5</td>
<td>9</td>
</tr>
<tr>
<td>ECASS II</td>
<td>0 – 6</td>
<td>11</td>
</tr>
<tr>
<td>NINDS</td>
<td>0 – 3</td>
<td>14</td>
</tr>
<tr>
<td>On site / Telemedicine</td>
<td>0 – 3</td>
<td>12/ 12.5</td>
</tr>
</tbody>
</table>

*Based on 148 patients data

mRS* (Modified Rankin Scale): functional scale from 0 (full recovery) to 6 (death)
Telestroke
Queen Elizabeth Hospital Hong Kong

- Managed by internists on site
- Telephone consultation + teleradiology
- Longer door to needle time
- Safety (sICH) and three month functional outcome is comparable to cases managed by neurologist on site
Feasibility and Safety of Remote Radiology Interpretation with telephone consultation for acute stroke in Thailand

• Managed by internal medicine resident on-duty
• Telephone consultation + teleradiology
• 100 patients treated with iv thrombolysis
• NIHSS: 15, Door to needle time: 54 minute
• SICH: 2%, 3-month mRS 0-1: 42%
## Comparison of Telestroke Cohorts

<table>
<thead>
<tr>
<th></th>
<th>TEMPiS</th>
<th>Zaidi</th>
<th>MGH</th>
<th>Finland</th>
<th>QEH</th>
<th>Thailand</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>106</td>
<td>83</td>
<td>181</td>
<td>61</td>
<td>50</td>
<td>100</td>
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<tr>
<td>Age</td>
<td>68</td>
<td>71.9</td>
<td>71.5</td>
<td>70</td>
<td>65</td>
<td>NA</td>
</tr>
<tr>
<td>Median NIHSS</td>
<td>13</td>
<td>12</td>
<td>13</td>
<td>10</td>
<td>12.5</td>
<td>15</td>
</tr>
<tr>
<td>Door to Needle time</td>
<td>76</td>
<td>89.9</td>
<td>NA</td>
<td>NA</td>
<td>96.5</td>
<td>54</td>
</tr>
<tr>
<td>Onset to Needle time</td>
<td>141</td>
<td>145.5</td>
<td>140</td>
<td>130</td>
<td>147.5</td>
<td>160</td>
</tr>
<tr>
<td>sICH (%)</td>
<td>8.5</td>
<td>1.2</td>
<td>3.9</td>
<td>6.7</td>
<td>4.0</td>
<td>2.0</td>
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<tr>
<td>mRS 0-1 (%)</td>
<td>NA</td>
<td>34.9</td>
<td>31</td>
<td>29.4</td>
<td>52.1</td>
<td>42</td>
</tr>
<tr>
<td>mRS 0-2 (%)</td>
<td>NA</td>
<td>42.1</td>
<td>NA</td>
<td>49.1</td>
<td>58.3</td>
<td>NA</td>
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</table>
Conclusion

• Telestroke increases accessibility to a 24/7 stroke thrombolysis service.

• Role of internists is critical.

• With internist’ support, telestroke model in QEH had achieved similar safety and outcome data as compared to direct management by neurologists.

• 24-hr IV stroke thrombolysis program in QEH is effective and safe. And outcome is comparable with oversea cohorts.
Stroke Thrombolysis Team
Acknowledgment

• All Internal Medicine Specialists involving in the screening & management of stroke patients with potentials for thrombolytic therapy

• All A&E physicians who had triggered the stroke thrombolysis call

• All Radiologists who provided timely neuroimaging

• All Nursing staffs who had provide nursing care and monitoring of those patients
Thank You