Evaluation of a Telephone Advice System for Remote Intravenous Thrombolysis in Ischemic Stroke

Data From a United Kingdom Network

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**Background and Purpose**—There is limited evidence for remote stroke thrombolysis using telephone consultation and teleradiology. Results from a UK network using this treatment model are presented.

**Methods**—Retrospective study of consecutive patients thrombolysed in 5 hospitals, with well organized stroke services, between 2012 and 2013. Remote thrombolysis was compared with thrombolysis delivered in person for symptomatic intracerebral hemorrhage, death within 7 days, and 90-day modified Rankin scores.

**Results**—Of 586 patients, 220 (37.5%) were thrombolysed remotely. The 2 groups were well matched (median age 77 years, NIHSS 12). Remote thrombolysis increased treatment time by 22 minutes. Outcomes were no different in the 2 groups (remote versus standard): symptomatic intracerebral hemorrhage (3.6% versus 4.6%), death within 7 days (6.4% versus 7.1%), modified Rankin score <2 (46.0% versus 46.1%), and modified Rankin score 6 (15% versus 17.5%) at 90 days.

**Conclusion**—Telephone advice and teleradiology, within an organized system of care, can be an effective method of delivery of intravenous thrombolysis. (Stroke. 2015;46:867-869. DOI: 10.1161/STROKEAHA.114.008190.)

**Key Words:** stroke ▪ telemedicine ▪ thrombolysis

Telesroke, video teleconferencing to support remote stroke interventions, has been endorsed in guidelines of thrombolysis for acute ischemic stroke. Studies of telesroke suggest similar mortality, intracerebral hemorrhage rates, and outcomes in comparison to trials and usual clinical practice. Data for thrombolysis using telephone consultation are limited. In a randomized study of telesroke versus telephone consultation, correct treatment decisions were made more often with telesroke but with no difference in adverse events. A single center study in the United Kingdom of telephone advice with teleradiology showed similar outcomes between patients treated remotely or in person. We present the results of a larger cohort of patients treated within a regional UK stroke network using telephone advice and teleradiology.

**Methods**

The Avon, Gloucestershire, Wiltshire, and Somerset Stroke Network covers 2.25 million people in south west England. Seven hospitals participate in a remote (out of hours) thrombolysis rota. All hospitals have stroke units, stroke specialists, and emergency physicians who provide in-house thrombolysis. There is a network-wide thrombolysis protocol and a training program based on the Safe Implementation of Treatments in Stroke training. Potential patients enter a standard pathway; treatment decisions are made by the on call remote thrombolysis consultant (one of 10 stroke physicians and 1 neurologist) after a telephone discussion with the in-house thrombolysis-certified clinician via a structured checklist. National Institute of Health Stroke Scale (NIHSS) scoring is reviewed and CT head viewed remotely by the on call clinician. The time window is 4.5 hours (details in the online-only Data Supplement).

A cohort of ≥100 consecutive patients from each center was retrospectively analyzed, comparing the remote group and patients thrombolysed in-house (standard group). Outcomes were Safe Implementation of Treatments in Stroke definition (hemorrhage with neurological deterioration >4 points on NIHSS or death within 7 days) symptomatic intracerebral hemorrhage, death (7 and 90 days), NIHSS scores at 24 and 7 days (or discharge if sooner), and modified Rankin score at 90 days dichotomized to good (0–2) and poor (3–6) outcomes. The Oxfordshire Community Stroke Project Classification was used to categorize strokes as total anterior circulation, partial anterior circulation, lacunar, and posterior circulation infarcts.

Student’s t test, Wilcoxon rank-sum test, or chi-squared tests were used as appropriate. The Cochran–Mantel–Haenszel Test was used for ordinal analysis of modified Rankin scores. Logistic regression models were used to identify predictors for symptomatic intracerebral hemorrhage and poor outcomes. Missing data were dealt with by complete case analysis for univariate statistics and multiple
ates showed no significant differences between the groups modified Rankin score scores without adjustment for covari-

The Cochran–Mantel–Haenszel Test for ordinal analysis of
comes, showing no significant difference between the groups.

Our study has the limitations of a retrospective cohort study. However, our patients were evenly matched for base-
line characteristics as the same protocol was followed for both standard and remote thrombolysis. We were not able to obtain data from 2 centers, thereby reducing the power of our study: one, a tertiary center, has no 3 month follow-up and the other could not collect the data required. We have no reason to sus-
pect any difference in case mix or outcomes in patients who
could not collect the data required. We have no reason to sus-
cept any difference in case mix or outcomes in patients who

(P<0.632). Baseline NIHSS score was the only consistent
determinant of poor outcomes in our logistic regression models.

Discussion

Our data suggest that delivering intravenous thrombolysis using
telephone consultation, teleradiology, and training of local clini-
cians is safe and effective in the context of stroke management
within hospitals with established stroke systems of care. This
model allowed 24/7 thrombolysis in our region, contributing to
a doubling in the number of patients treated between 2009 and
2013. In this series, 37.5% of patients were treated remotely and
47.8% treated outside office hours overall.

Remote treatment increased the door-to-needle time by 22
minutes, of which 14 minutes was related directly to the pro-
cess of remote consultation, whereas the rest could be attrib-
uted to slower processes outside office hours. Corresponding
increase in treatment times reported in the literature varies
from 8 to 22 minutes.5,6,8 NIHSS change, proportion who had
died by 3 months (16.6%) and the symptomatic intracerebral hemorrhage rate (4.2%) are comparable to other reports (Table in the online-only Data Supplement).6,8

Our study was the limitations of a retrospective cohort study. However, our patients were evenly matched for baseline characteristics as the same protocol was followed for both standard and remote thrombolysis. We were not able to obtain data from 2 centers, thereby reducing the power of our study: one, a tertiary center, has no 3 month follow-up and the other could not collect the data required. We have no reason to suspect any difference in case mix or outcomes in patients who received treatment in the 2 missing centers based on internal network audits. Missing data were minimal and dealt with by standard statistical techniques. Our results, however, cannot be widely generalized to other healthcare settings.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Standard Thrombolysis (n=366)</th>
<th>Remote Thrombolysis (n=220)</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>78</td>
<td>76</td>
<td>0.123</td>
</tr>
<tr>
<td>Sex (% of males)</td>
<td>51.9%</td>
<td>49.1%</td>
<td>0.564</td>
</tr>
<tr>
<td>Previous stroke/TIA, %</td>
<td>23.8%</td>
<td>29.1%</td>
<td>0.184</td>
</tr>
<tr>
<td>Other risk factors, %</td>
<td>75.7%</td>
<td>76.8%</td>
<td>0.832</td>
</tr>
<tr>
<td>PAF/AF, %</td>
<td>33.9%</td>
<td>30.0%</td>
<td>0.378</td>
</tr>
<tr>
<td>Other serious comorbidities, %</td>
<td>22.1%</td>
<td>21.8%</td>
<td>1</td>
</tr>
<tr>
<td>TACI</td>
<td>45.6%</td>
<td>42.3%</td>
<td>0.6314</td>
</tr>
<tr>
<td>PACI</td>
<td>40.4%</td>
<td>40.5%</td>
<td></td>
</tr>
<tr>
<td>LACI</td>
<td>7.9%</td>
<td>11.8%</td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>3.0%</td>
<td>3.2%</td>
<td></td>
</tr>
<tr>
<td>Baseline NIHSS (median)</td>
<td>12</td>
<td>12.5</td>
<td>0.835</td>
</tr>
<tr>
<td>Baseline mRS (median)</td>
<td>0</td>
<td>0</td>
<td>0.549</td>
</tr>
<tr>
<td>Thrombolysed out of hours, %</td>
<td>20.2%</td>
<td>93.6%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; LACI, lacunar anterior circulation infarct; mRS, modified Rankin; OCSP, Oxfordshire Community Stroke Project; PACI, partial anterior circulation infarct; PAF, paroxysmal atrial fibrillation; POCI, posterior circulation infarct; TACI, total anterior circulation infarct; and TIA, transient ischemic attack.

Table 2. Treatment Times and Outcomes With 95% Confidence Intervals

<table>
<thead>
<tr>
<th></th>
<th>Standard Thrombolysis (n=366)</th>
<th>Remote Thrombolysis (n=220)</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean door to needle time, min</td>
<td>53.7 (50.9–56.5)</td>
<td>76.6 (72.2–80.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean onset to needle time, min</td>
<td>139.5 (134.5–144.4)</td>
<td>161.6 (154.9–168.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median NIHSS change at 24 h</td>
<td>-5 (4.5–6.0)</td>
<td>-5.4 (4.5–6.0)</td>
<td>0.9014</td>
</tr>
<tr>
<td>Median NIHSS change by discharge or 7 days</td>
<td>-8.5 (7.5–9.0)</td>
<td>-8.5 (6.9–9.5)</td>
<td>0.835</td>
</tr>
<tr>
<td>SICH, %</td>
<td>4.6% (2.7–7.3)</td>
<td>3.6% (1.6–7)</td>
<td>0.7085</td>
</tr>
<tr>
<td>Death within 7 days, %</td>
<td>7.1% (4.7–10.2)</td>
<td>6.4% (3.5–10.4)</td>
<td>0.8612</td>
</tr>
<tr>
<td>Death within 3 months, %</td>
<td>17.5% (13.7–21.8)</td>
<td>15.0% (10.6–20.4)</td>
<td>0.5032</td>
</tr>
<tr>
<td>Good outcome (mRS 0–2)</td>
<td>46.1% (41.0–51.8)</td>
<td>46.0% (39.2–53.4)</td>
<td>1</td>
</tr>
<tr>
<td>Protocol violations, %</td>
<td>4.1% (2.3–6.7)</td>
<td>3.6% (1.6–7.0)</td>
<td>0.9528</td>
</tr>
<tr>
<td>r-tPA complications excluding SICH</td>
<td>8.7% (6.1–12.1)</td>
<td>10.9% (7.1–15.8)</td>
<td>0.4724</td>
</tr>
</tbody>
</table>

mRS indicates modified Rankin; NIHSS, National Institute of Health Stroke Scale; r-tPA, recombinant tissue-type plasminogen activator; SICH, symptomatic intracerebral hemorrhage; and TIA, transient ischemic attack.

Data from 586 patients from 5 hospitals thrombolysed between January 2012 and December 2013 were available. Two hundred twenty patients (37.5%) were thrombolysed remotely and 366 patients received standard thrombolysis. Median age was 77 years (interquartile range, 68–84) and 50.9% were male. 37% were >80 years of age. The proportion of strokes thrombolysed by these hospitals was ≈10% of all strokes admitted in 2013. The door-to-needle time was missing in 1.9%, onset-to-needle time in 1.4%, and 3 month modified Rankin score missing in 7% of cases. All NIHSS scores, symptomatic intracerebral hemorrhage, and deaths were complete. An assumption of data missing at random was made because the proportion of missing items was similar in both groups.

Baseline median NIHSS was 12.3 (interquartile range, 8–18). The groups were well matched for baseline characteristics (Table 1), but more patients were thrombolysed out of hours (18:00–08:00) by remote guidance. Mean onset-to-needle time was 147.7 minutes (SD 49.7) for the whole cohort. 47.8% were thrombolysed outside office hours. Telephone advice increased door-to-needle time by 22 minutes (Table 2). Patients treated outside office hours without remote support had door-to-needle time 8 minutes greater than those within hours.

Table 2 compares the standard and remote groups for all out-
comes, showing no significant difference between the groups.

The Cochran–Mantel–Haenszel Test for ordinal analysis of modified Rankin score scores without adjustment for covari-

AF indicates atrial fibrillation; LACI, lacunar anterior circulation infarct; mRS, modified Rankin; OCSP, Oxfordshire Community Stroke Project; PACI, partial anterior circulation infarct; PAF, paroxysmal atrial fibrillation; POCI, posterior circulation infarct; TACI, total anterior circulation infarct; and TIA, transient ischemic attack.
In summary, given comparable clinical settings, where telestroke is not possible, implementing a service delivery model such as ours may enable more patients to benefit from thrombolysis for acute ischemic stroke.

Disclosures
K. Hellier has accepted conference sponsorship and an honorarium for a lecture from Boehringer-Ingelheim. The other authors report no conflicts.

References
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SUPPLEMENTAL MATERIAL

Supplemental Methods

Characteristics of the centers

The network includes a mixture of rural and urban communities and includes nine acute district general hospitals (one of which is a tertiary stroke center) and one ambulance service. Seven hospitals participate in a remote thrombolysis rota. All the hospitals are medium to large in size and have stroke units and stroke specialists who provide in-house thrombolysis within hours. All have major emergency departments with thrombolysis trained and experienced emergency physicians who can thrombolyse independently with or without image interpretation support. There is a Network-wide thrombolysis clinical protocol based on the National Institute of Neurological Disorders protocol and a clinician training programme based on the Safe Implementation of Treatments in Stroke (SITS) and British Association of Stroke Physicians (BASP) training. The Network telemedicine rota and thrombolysis protocol have been implemented successfully and have been running for approximately 5 years. Clinical governance and indemnity procedures are in place.

Process of remote thrombolysis

A rota of 10 stroke physicians and one neurologist covers the whole area when on call. The on call specialists are drawn from all participating hospitals and not just from the tertiary stroke center. Several of the emergency departments use the Recognition of Stroke in the Emergency Room (ROSIER) tool and paramedics use the Face Arm and Speech Test (FAST) to screen patients with possible stroke. The treatment time window was increased from 3 to 4.5 hours in 2012. When suitable patients are identified, they enter a structured thrombolysis pathway which uses documentation identical for the whole network. Thrombolysis treatment decisions are made by the on call “remote” clinician after a discussion with the local “in-house” thrombolysis-certified clinician via a structured checklist. The NIHSS scoring is reviewed by discussion over the phone and the CT head viewed remotely by the on call clinician. No radiologists are involved in reporting out of hours. All centers use plain CT as the basis for thrombolysis decisions. There is no upper age limit and active blood pressure lowering before administration of rt-Pa is allowed by a Network-wide standard protocol. Thrombolysed patients are managed according to a standard post-thrombolysis protocol on acute stroke units with in-house senior stroke specialist review the next morning. Almost all patients have a follow up CT at 24 – 48 hours even if there is no neurological deterioration. Most centres have a system of regular feedback on treated and missed cases with ED and remote clinicians.
Supplemental results

**Supplemental Table I:** comparison of averaged results of both arms of this and other telemedicine studies and SITS-UK results.

<table>
<thead>
<tr>
<th></th>
<th>This study (n=586)</th>
<th>Northumbria 4 (n=178)</th>
<th>Pittsburgh 5 (n=142)</th>
<th>UK-SIT 1 (n=614)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>77</td>
<td>75.4</td>
<td>71.9 (mean)</td>
<td>68 years (median)</td>
</tr>
<tr>
<td>Baseline NIHSS (IQR 8-18)</td>
<td>13.3</td>
<td>13.5</td>
<td>11.3</td>
<td>14.5 (IQR 9-19)</td>
</tr>
<tr>
<td>Thrombolysis window</td>
<td>Up to 4.5 hrs</td>
<td>Up to 4.5 hrs</td>
<td>Not stated</td>
<td>Up to 3 hrs</td>
</tr>
<tr>
<td>Increase in door to needle time in remote thrombolysis group</td>
<td>22 minutes (mean)</td>
<td>8 minutes (median)</td>
<td>22 minutes (mean)</td>
<td>N/A</td>
</tr>
<tr>
<td>NIHSS change at 7d</td>
<td>-8.5 (7.5-9.0)</td>
<td>-7.5 (4-11)</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Good outcomes at 3 months</td>
<td>46% (mRS 0-2)</td>
<td>51.5% (mRS 0-2)</td>
<td>40% (mRS 0-2)</td>
<td>43% (mRS 0-2)</td>
</tr>
<tr>
<td>SICH</td>
<td>4.1%</td>
<td>2%</td>
<td>3.2%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Death within 7 days</td>
<td>6.8%</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Death at 3 months</td>
<td>16.3%</td>
<td>18.9%</td>
<td>31%</td>
<td>21%</td>
</tr>
</tbody>
</table>

**References**