Stroke Thrombolysis in a Centralized and a Decentralized System (Helsinki and Telemedical Project for Integrative Stroke Care Network)

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Background and Purpose—Intravenous thrombolysis with tissue-type plasminogen activator (tPA) for acute ischemic stroke is more effective when delivered early. Timely delivery is challenging particularly in rural areas with long distances. We compared delays and treatment rates of a large, decentralized telemedicine-based system and a well-organized, large, centralized single-hospital system.

Methods—We analyzed the centralized system of the Helsinki University Central Hospital (Helsinki and Province of Uusimaa, Finland, 1.56 million inhabitants, 9096 km²) and the decentralized TeleStroke Unit network in a predominantly rural area (Telemedical Project for Integrative Stroke Care [TEMPiS], South-East Bavaria, Germany, 1.94 million inhabitants, 14992 km²). All consecutive tPA treatments were prospectively registered. We compared tPA rates per total ischemic stroke admissions in the Helsinki and TEMPiS catchment areas. For delay comparisons, we excluded patients with basilar artery occlusions, in-hospital strokes, and those being treated after 270 minutes.

Results—From January 1, 2011, to December 31, 2013, 912 patients received tPA in Helsinki University Central Hospital and 1779 in TEMPiS hospitals. Area-based tPA rates were equal (13.0% of 7017 ischemic strokes in the Helsinki University Central Hospital area versus 13.3% of 14637 ischemic strokes in the TEMPiS area; P=0.078). Median prehospital delays were longer (88; interquartile range, 60–135 versus 65: 48–101 minutes; P<0.001) but in-hospital delays were shorter (18; interquartile range, 13–30 versus 39; 26–56 minutes; P<0.001) in Helsinki University Central Hospital compared with TEMPiS with no difference in overall delays (117; interquartile range, 81–168 versus 115; 87–155 minutes; P=0.45).

Conclusions—A decentralized telestroke thrombolysis service can achieve similar treatment rates and time delays for a rural population as a centralized system can achieve for an urban population. (Stroke. 2016;47:2999-3004. DOI: 10.1161/STROKEAHA.116.014258.)

Key Words: delivery of health care ■ stroke ■ telemedicine ■ telestroke ■ thrombolysis ■ time delays
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patients treated per hospital is usually smaller. Door-to-needle times seem to have an inverse relationship to the annual number of patients with stroke per hospital, suggesting experience of the team as a crucial factor for achieving short in-hospital delays.5,12,13 Thus, a decentralized system may lead to longer in-hospital time delays.

The aim of this study was to determine whether a decentralized model of stroke care (TEMPiS) can achieve similar thrombolysis rates and overall treatment delays in a predominantly rural population compared with the centralized system in Helsinki and the province of Uusimaa.

Methods

We performed an observational retrospective cohort study with prospectively collected data and a prespecified analysis plan.

Helsinki University Central Hospital Setup

The Health District of Helsinki and Uusimaa covers public specialist care in the province of Uusimaa (Figure). In 2011 to 2013, the province had a mean population of 1.56 million and a surface area of 9096 km². The whole area is defined as urban by the NUTS3 definition of the European Union (Nomenclature of Units for Territorial Statistics–level 3, for small regions), because of the therein embedded metropolitan region of Helsinki.15

The Helsinki thrombolysis service has been described previously.5 Briefly, HUCH is the only hospital in the province providing thrombolysis for stroke. All potentially eligible patients with stroke are brought to this 1 large hospital 24 hours/d, 7 days/wk. Although the driving distance can be up to 90 minutes, most of the population lives in the metropolitan area, typically within a 30-minute driving distance of HUCH. The province-wide ambulance service contacts the HUCH stroke consultant directly over mobile phone for any patient with a possible stroke to discuss patient details, medical history, and tPA eligibility during transport. Before the patient’s arrival, the stroke consultant accesses previous medical records, imaging, and laboratory test results available in electronic format in a province-wide patient record; preregisters the patient into the hospital, requests blood tests and imaging, and assembles the team to wait for the patient. Because of concentrated resources of a centralized system, there is a neurology resident and a specialist neurologist in the hospital 24/7. The Helsinki model has been developed over many years and includes constant collaboration and training of the emergency medical services, continuous quality improvement utilizing the prospective thrombolysis registry, and a systematic training program within the stroke team. The history of the quality improvement program has been described in detail previously.5

Telestroke Network TEMPiS Setup

The TEMPiS network covers stroke specialist care in 14 districts in South-East Bavaria (Figure). In 2011 to 2013, the districts had a mean population of 1.94 million and a surface area of 14 992 km².16 Nine of the districts are defined as rural and 5 as intermediate by the NUTS3 definition of the European Union.15 The network has been described previously.10,17 Briefly, it consists of 2 hub centers (Munich/Klinikum Harlaching and Regensburg/University Hospital) and 14 (in 2011) or 15 (in 2012 and 2013) cooperating TEMPiS spoke hospitals, each covering their administrative district in South-East Bavaria, Germany (Figure). The network was set up with the aim that patients do not have a driving distance of >30 minutes to a (Tele-) Stroke Unit. As part of the TEMPiS concept, regular training sessions for the multidisciplinary teams, internal registries, and standard operating procedures were established. The 24/7 teleconsultation service includes real-time bidirectional videoconference and imaging transfer. Continuous stroke-specific program performed by hub centers for spoke hospital staff includes semiannual stroke updates, semiannual full-day stroke beginners courses, and annual full-day conference days for nurses and therapists. Stroke awareness campaigns and stroke-specific

Figure. Geographical catchment area, degree of urbanization, and location of stroke units in the Uusimaa province, Finland, and the Telemedical Project for Integrative Stroke Care (TEMPiS) network, Germany. Adapted and modified from EuroStat maps.14 Including OpenData License permission of © EuroGeographics. Original product is freely available at www.eurogeographics.org. Terms of the license available at http://www.eurogeographics.org/form/topographical-data-eurogeographics. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.
training of emergency medical services are performed annually by each TEMPiS hospital for their own district. Process improvement programs performed by hub centers include regular analyses of collected data sets for each hospital, annual comprehensive feedback documents including improvement plans and semiannual audits in each spoke hospital. Ambulances are usually staffed with 2 paramedics. Emergency physician maybe deployed in critically ill patients. Patients with suspicion of stroke are to be brought to closest hospital with Stroke Unit. Paramedics are trained in stroke recognition during professional training and in the above-mentioned training.

Four of the TEMPiS hospitals have a Neurology service 24/7, and telemedicine is used in these hospitals mainly for the second opinion and organization of emergency transports. Three hospitals use a full-time neurologist during working hours. Neurological expertise is provided by part-time neurologists during working hours in all other hospitals. Among other indications, video presentation of patients with acute stroke potentially eligible for thrombolysis is mandatory if no neurologist is available at the bedside. If a neurologist is available onsite, thrombolysis may be delivered without telemedicine assistance. This was the case in about one third of the patients. Brief medical history, noncontrast CT scan, blood pressure measuring, and blood sampling are performed before the start of videoconference. If tPA is recommended, administration commences directly after videoconference. Within the districts covered by TEMPiS, 2 other hospitals (not part of the network) offer Stroke Unit service (Wasserburg and Bad Aibling) including tPA treatment.

Data Collection
All data used in this article were prospectively collected from patients who received intravenous tPA between January 1, 2011, and December 31, 2013, in HUCH and in the TEMPiS spoke hospitals. The Helsinki Stroke Thrombolysis Registry has recorded all intravenous tPA deliveries at HUCH since 1995. The total number of ischemic stroke admissions was taken from the HUCH administrative records and included all admissions to emergency department with a final discharge diagnosis of ischemic stroke (International Classification of Diseases-Tenth Revision I63), whether the patients were treated under neurology or any other discipline. The population-based ischemic stroke numbers were estimated from the Finnish national stroke registry PERFECT (Performance, Effectiveness, and Cost of Treatment Episodes in Stroke), which uses administrative data linkage to identify in addition to admissions to the major hospital also cases managed at health centers and in the private sector. The Helsinki Stroke Thrombolysis Registry includes all patients with acute ischemic stroke treated with intravenous thrombolysis in any of the TEMPiS hospitals. Neither data of the 2 hub centers and their catchment areas nor data of adjacent non-network districts were included in the current analysis. One spoke TEMPiS hospital (Pasing) is located in the city of Munich with overlapping catchment areas of the hub center and other non-network Stroke Units and was therefore excluded from this analysis. One spoke TEMPIS hospital (Bad Reichenhall) joined the network end of 2011, and data were therefore only included for the years 2012 and 2013. Two other hospitals joined the network end of 2013 and were therefore not included in this analysis. Hence, data for 13 (for 2011) and 14 (for 2012–2013) TEMPIS hospitals were included. Tests for plausibility and comparisons to other TEMPIS registries are regularly performed. To calculate area-based thrombolysis rate, the 2 non-network Stroke Units within the districts covered by TEMPIS provided numbers of tPA administrations in their hospitals. Numbers of ischemic stroke admissions in the whole area (including non-network hospitals, but excluding the catchment areas of the hubs and the spoke hospital Pasing) were gathered from the official quality reports of all hospitals providing acute care within the TEMPIS districts (n=32) for 2011 to 2013 and were confirmed by the Bavarian health government (data collected by the Institut für das Entgeltsystem im Krankenhaus, InEK GmbH, Germany).

Hospital-based tPA rate was defined as all patients with acute ischemic stroke treated with tPA in the given hospital (numerator) of all available onsite, thrombolysis may be delivered without telemedicine assistance. This was the case in about one third of the patients. Brief medical history, noncontrast CT scan, blood pressure measuring, and blood sampling are performed before the start of videoconference. If tPA is recommended, administration commences directly after videoconference. Within the districts covered by TEMPiS, 2 other hospitals (not part of the network) offer Stroke Unit service (Wasserburg and Bad Aibling) including tPA treatment.

<table>
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<tr>
<th>Table 1. Regional Characteristics, Number of Acute Ischemic Stroke Admissions and Number of tPA Treatments for 2011 to 2013</th>
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<tbody>
<tr>
<td><strong>Regional characteristics</strong></td>
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<tr>
<td>Inhabitants living in the area</td>
</tr>
<tr>
<td>Surface area, km²</td>
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<tr>
<td>Population density, population/km²</td>
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<tr>
<td>Characteristics of patients treated with tPA</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
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<tr>
<td>Sex, women (%)</td>
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<tr>
<td>NIHSS, median (IQR)</td>
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Table 2. Exclusion Profile for Time Delay Analysis

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<td>Table 1. Regional Characteristics, Number of Acute Ischemic Stroke Admissions and Number of tPA Treatments for 2011 to 2013</td>
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<tr>
<td><strong>Hospital-based tPA rate</strong></td>
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<tr>
<td>In-hospital strokes, n (%)</td>
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<tr>
<td>Basilar artery occlusions, n (%)</td>
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<tr>
<td>Onset-to-treatment time &gt;270 min, n (%)</td>
</tr>
<tr>
<td>Missing data, n (%)</td>
</tr>
<tr>
<td>Included in time delay analyses, n (%)</td>
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</tbody>
</table>

Exclusions were performed following the criteria top to bottom. TEMPIS indicates the Telemedical Project for Integrative Stroke Care.
patients with acute ischemic stroke admitted to this hospital (denominator). Area-based tPA rate was defined as all patients with acute ischemic stroke treated with tPA in the given hospital (nominator) of all patients with acute ischemic stroke admitted to any hospital within the catchment area of this hospital (denominator).

Data sets from patients with in-hospital stroke or basilar artery occlusion and from patients treated after 270 minutes from onset or with incomplete information on time points were not included in time delay analyses. A sensitivity analysis was performed, in which patients with basilar artery occlusion and in-hospital stroke were included.

Both registries were approved as observational quality registries, patient consent was not required for registration, and all consecutive cases were included.

### Statistical Analysis

Because of non-normal distribution of treatment delays, data are presented as median and interquartile range. The data of the 2 registries were compared using Mann–Whitney U test for continuous and Pearson χ² test for dichotomous data. Statistical significance was set at 0.05 (2 tailed). No adjustment for multiple testing was done. IBM SPSS Statistics 23 (IBM Corp, Armonk, NY) was used for all analyses.

### Results

Geographical and patients’ characteristics, as well as thrombolysis rates, are shown in Table 1. During the study period, 912 and 1779 patients with stroke were treated with tPA in HUCH and TEMPiS, respectively. Hospital-based annual tPA rates ranged between 7.5% and 20% in the TEMPiS hospitals. Hospital-based tPA rate in HUCH was higher than overall tPA rate in TEMPiS hospitals (26.9% versus 15.4%; \( P<0.001 \)). However, there was no statistically significant difference in area-based tPA rates between the areas covered by HUCH and TEMPiS spoke hospitals (13.0% versus 13.3%; \( P=0.078 \)). Exclusions for the time delay analysis are shown in Table 2 and time delays in Table 3. Onset-to-door time was significantly longer (88 [60–135] versus 65 [48–101] minutes; \( P<0.001 \)) and door-to-needle time significantly shorter (18 [13–30] versus 39 [26–56] minutes; \( P<0.001 \)) in HUCH versus TEMPiS. Overall onset-to-treatment time was equal (117 [81–168] versus 115 [87–155] minutes; \( P=0.452 \)). These results remained similar when patients with basilar artery occlusions and in-hospital strokes were included in the analysis (Table 4).

### Discussion

Our comparison of 2 systems of stroke care shows that a decentralized telemedicine-supported infrastructure can achieve similar thrombolysis rates and overall time delays in a rural population as a centralized system can achieve in an urban population.

The different catchment areas (urban versus rural) may explain the age difference of the 2 patient groups. The difference in mean NIHSS (National Institute of Health Stroke Scale) is unclear, as in neither system very low or high NIHSS is considered a clear contraindication.

Although hospital-based tPA rate was much higher in HUCH than in TEMPiS, area-based tPA rate was similar in both systems. This difference is explained by the prehospital selection of patients with stroke in Helsinki/Uusimaa. Patients eligible for thrombolysis are transferred to HUCH, whereas others may also be treated in a local hospital without a Stroke Unit. This is also reflected by the lower rate of dedicated Stroke Unit treatments in Helsinki/Uusimaa (48%; Table 1). Most of the patients treated outside of HUCH are treated under neurology with typically half of the beds used for patients with stroke but not within a dedicated Stroke Monitoring Unit. In the TEMPiS system, prehospital selection is less frequent, as network hospitals are the local hospitals, close to patients’ homes. Only few patients are admitted to other hospitals. As a result, 88% of patients with stroke are treated in hospitals with a (Tele-)Stroke Unit.

The only previous comparison of centralized and decentralized tPA systems of care found a higher hospital-based tPA rate in the centralized system (n=175), but a selection bias cannot be excluded because fewer patients with stroke were admitted to the stroke center of the centralized system (49 compared with 70 per 100000 inhabitants), and these patients

### Table 3. Time Delays (in Minutes)

<table>
<thead>
<tr>
<th></th>
<th>Helsinki (n=826)</th>
<th>TEMPiS (n=1600)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset-to-door time</td>
<td>88 (60–135); 105±55.9</td>
<td>65 (48–101); 80.1±45.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Door-to-needle time</td>
<td>18 (13–30); 25.1±20.0</td>
<td>39 (26–56); 44.7±26.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Onset-to-treatment time</td>
<td>117 (81–168); 130±59.1</td>
<td>115 (87–155); 124.8±49.4</td>
<td>0.452</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range; and TEMPiS, the Telemedical Project for Integrative Stroke Care; and tPA, tissue-type plasminogen activator.

### Table 4. Sensitivity Analysis for Time Delays (in Minutes) With All Patients, Except With Missing Data and Treated >270 Minutes After Onset

<table>
<thead>
<tr>
<th></th>
<th>Helsinki (n=861)*</th>
<th>TEMPiS (n=1733)†</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset-to-door time</td>
<td>88 (60–135); 104.9±56.0</td>
<td>65 (45–97); 75.3±47.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Door-to-needle time</td>
<td>18 (13–31); 25.8±21.3</td>
<td>40 (27–60); 48.5±33.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Onset-to-treatment time</td>
<td>118 (82–168); 130.8±59.0</td>
<td>115 (85–155); 123.7±50.8</td>
<td>0.141</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range; and TEMPiS, the Telemedical Project for Integrative Stroke Care.

*Excluded: n=50 with onset-to-treatment time >270 minutes, n=1 missing dates per time.
†Excluded n=27 with onset-to-treatment time >270 minutes, n=19 missing dates/time.
thrombolysis mortality in TEMPiS hospitals was 8.6%. This is almost identical to the overall Bavarian thrombolysis mortality rate (8.4%) and similar to the national registry in the United States (8.8%). Third, the emergency medical service may be organized differently in each system, influencing prehospital delay and prehospital selection. Fourth, alarm (or emergency call) time was not recorded in either of the 2 registries. Prealarm delay may be different in the 2 countries because of distinct stroke awareness, affecting overall delays beyond long distances to hospitals, thus limiting interpretation of prehospital delay. This should be studied in further prospective analyses. Fifth, as we have only included 1 system for each comparison, external validity is limited, as there are features that may be very network dependent. Also, some of the specific features of our 2 models of care may not be implementable in other settings because of different population densities, catchment areas, healthcare systems, and regional infrastructures. Comparison of 2 different systems of care is always challenging and bares many unknown and uncontrollable confounders. To increase validity, further multicenter comparison is warranted.

Conclusions

The results of our study indicate that a decentralized stroke system of care assisted by telemedicine can achieve equal thrombolysis treatment rates and onset-to-treatment delays in a predominantly rural, sparsely populated region as they are achieved in a mainly urban population with a centralized system.

Acknowledgments

We thank all staff members of Helsinki University Central Hospital and the participating hospitals in Telemedical Project for Integrative Stroke Care (TEMPiS) network that were involved in the care of our patients with stroke and all teleconsultants for their exceptional support of the network. We also thank the Institut für Medizinsoziologie, Versorgungsforschung und Rehabilitationsschwerpunkt der Humanwissenschaftlichen Fakultät der Medizinischen Fakultät der Universität zu Köln, Cologne, Germany, and the Bavarian Ministry of Health for providing data on overall stroke rate in the TEMPiS region. We also thank the Schön Klinik Bad Aibling and the kbo-Inn-Salzach-Klinikum Wasserburg for providing their data on tissue-type plasminogen activator treatments.

Disclosures

Dr Adebert received grants or personal fees from Center for Stroke Research Berlin and Boehringer-Ingelheim. Dr Tatlisumak received grants or personal fees from Helsinki University Central Hospital, Boehringer-Ingelheim, Mitsubishi Pharma, Baer, Pfizer, Lundbeck A/S, Sanofi Aventis, PhotoThera Inc, BransGate, Orion Pharma, Professio Finland outside the submitted work. Dr Boy received personal fees from Boehringer-Ingelheim, Pfizer, Bristol-Myers Squibb. Dr Kaste reports grants from Lundbeck A/S, Siemens AG, Mitsubishi Pharma outside the submitted work.

References


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Stroke. 2016;47:2999-3004; originally published online November 10, 2016; doi: 10.1161/STROKEAHA.116.014258

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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