Telemedicine for Safe and Extended Use of Thrombolysis in Stroke

The Telemedic Pilot Project for Integrative Stroke Care (TEMPiS) in Bavaria

Heinrich J. Audebert, MD; Christian Kukla, MD; Stephan Clarmann von Claranau, MD; Johannes Kühn, MD; Bijan Vatankhah, MD; Johannes Schenkel, MD; Guntram W. Ickenstein, MD; Roman L. Haberl, MD; Markus Horn, MD; on behalf of the TEMPiS Group

Background and Purpose—Systemic thrombolysis represents the only proven therapy for acute ischemic stroke, but safe treatment is reported only in established stroke units. One major goal of the ongoing Telemedic Pilot Project for Integrative Stroke Care (TEMPiS) in Bavaria is to extend the use of tissue plasminogen activator (tPA) treatment in nonurban areas through telemedic support.

Methods—The stroke centers in Munich-Harlaching and in Regensburg established a telestroke network to provide consultations for 12 local hospitals in eastern Bavaria. The telemedic system consists of a digital network that includes a 2-way video conference system and CT/MRI image transfer with a high-speed data transmission up to 2 Mb/s. Each network hospital established specialized stroke wards in which qualified teams treat acute stroke patients. Physicians in these hospitals are able to contact the stroke centers 24 hours per day.

Results—A total of 106 systemic thrombolyses were indicated via teleconsultations between February 1, 2003, and April 7, 2004. During the first 12 months, the rate of thrombolyses was 2.1% of all stroke patients. Mean age was 68 years, and median National Institutes of Health Stroke Scale score was 13. Mean delay between onset and hospital admission was 65 minutes, and door-to-needle time was on average 76 minutes, which included 15 minutes for the teleconsultation. Symptomatic hemorrhage occurred in 8.5% of patients, and in-hospital mortality was 10.4%.

Conclusions—The present data suggest that systemic thrombolysis indicated via stroke experts in the setting of teleconsultation exhibits similar complication rates to those reported in the National Institute of Neurological Disorders and Stroke trial. Therefore, tPA treatment is also safe in this context and can be extended to nonurban areas. (Stroke. 2005;36:287-291.)

Key Words: acute care • cerebral infarct • complications • economics • intracerebral hemorrhage • stroke management • thrombolysis • remote evaluation • telemedicine • telestroke

Tissue plasminogen activator (tPA) thrombolysis remains the only available causal therapy of acute ischemic stroke. Although this treatment was approved in the United States in 1996 and in Europe in 2002, this therapeutic option is offered mainly in academic stroke centers. The overall percentage of systemic thrombolysis is reported to be below 5%.

The major reason patients do not receive intravenous thrombolytic therapy is arrival at a stroke treatment center after the 3-hour time window. In rural areas, long distances prevent timely admission of patients to fully equipped centers. On the other hand, experience with thrombolysis in local hospitals without specialized expertise revealed increased complication rates. Therefore, international guidelines suggest that "thrombolytic therapy should only be given if the diagnosis is established by a physician who has expertise in the diagnosis of stroke, and a CT of the brain is assessed by physicians who have expertise in reading this imaging study."

The Telemedic Pilot Project for Integrative Stroke Care (TEMPiS) was designed to make specialized stroke therapy available for patients in rural areas, with a special focus on systemic thrombolysis. This study investigates the procedural quality and safety of tPA administration when used in local hospitals after telemedic evaluation.

Methods

TEMPiS was founded by 2 comprehensive stroke centers in Munich Harlaching and Regensburg to provide consultation to 12 regional clinics in eastern Bavaria. None of the regional hospitals had a stroke...
Two hospitals have a neurological department, and the other 10 hospitals are participating with their general internal medicine departments. The location of the 2 stroke centers and the distances to the regional hospitals are shown in the Figure.

The TEMPiS concept is based on 4 key elements: (1) specialized stroke wards in each hospital (24-hour availability of diagnostics; stroke teams; standardized stroke care protocols); comprehensive and continuing stroke training for all medical staff members; (3) telemedicine network (with 24-hour service, on a week-by-week rotation, with 5 full-time experienced neurologists specializing in stroke and with high-speed data transmission); and (4) central organization of interhospital transfers. For use of tPA, an intensive education program was conducted in the local hospitals that included training regarding the National Institutes of Health Stroke Scale (NIHSS), implementation of a thrombolysis algorithm, and disposition of tPA protocols.

These protocols include inclusion and exclusion criteria, the NIHSS, and instructions for treatment and monitoring of patients. The guidelines for this treatment are based on the European approval definitions that permit tPA administration within 3 hours of stroke onset and for patients with chronically relevant neurological deficit (eg at least 5 points on the NIHSS). For safety reasons, the upper limit of the NIHSS was restricted to 20 points. The protocols had to be completed by the attending doctors of the local hospitals, who fixed the exact time course. To facilitate the use of tPA, a stroke code box, which contained all necessary tools and medications, was distributed in all hospitals.

When patients were admitted to the local clinic with a possible indication for systemic thrombolysis, they were immediately screened by the attending doctors. During the CT investigation, the telemedic consultant was informed by telephone. The CT scans, which had already been transmitted to the local telemedicine workstation (via LAN), were retrieved at the workstation of the stroke center. The retrieval of a complete head scan took approximately 2 minutes. After evaluation of the CT scans, the videoconference was begun, focusing on the clinical examination based on the NIHSS. The investigation was assisted by the attending physicians of the regional hospitals. After a final check of possible exclusion criteria, it was determined whether the patient was eligible for thrombolysis. It was recommended that the tPA bolus be administered in the teleconference room and that perfusion of tPA was then performed either in the intensive care unit or in the intermediate care unit.

All patients were prospectively enrolled in the safety analysis. Data were documented in the tPA protocols and in the databank of the telemedicine service. In-hospital mortality and length of hospital stay were determined by the discharge reports. To detect intracranial hemorrhage, CT scans were required by protocol at 24 hours and when any clinical deterioration occurred. For analysis of intracranial hemorrhages, CT scans were collected and evaluated by a radiologist blinded to the clinical course.

Bleedings were categorized according to the criteria published by Fiorelli et al for the European Cooperative Acute Stroke Study I (ECASS I) cohort: (1) hemorrhagic infarctions with small petechial hematoma (HI1); (2) hemorrhagic infarctions with more confluent petechiae (HI2); (3) parenchymal hematoma <30% of the infarcted area with some mild space-occupying effect (PH1); and (4) parenchymal hematoma ≥30% of the infarcted area with significant space-occupying effect or clot remote from infarcted area (PH2). In addition, the term “focal subarachnoid hemorrhage” was used by the radiologist for a small subarachnoid hemorrhage in 1 hemispheric sulcus next to the infarcted area without extension to other sulci or basal cisterns.

According to the National Institute of Neurological Disorders and Stroke (NINDS) definition, hemorrhage was considered symptom-
atic “if it was not seen on a previous CT scan and there had subsequently been either a suspicion of hemorrhage and any decline of neurologic status.” For comparison of the samples, intracerebral hemorrhages were assessed as treatment related when they occurred within 36 hours. Interim analysis for safety assessment was performed after 42 systemic thrombolyses.

Statistical Analysis
Data were analyzed with the Statistical Package for Social Sciences (SPSS). Values were expressed as mean±SD or medians, and comparisons between groups with and without protocol deviations were performed with the Fisher exact test. Safety data were compared with historical controls with the χ² test.

Results
Between February 1, 2003, and April 7, 2004, a total of 106 patients received systemic thrombolysis after telemedicine assessment. Data for 356 patients with a possible indication for thrombolysis were presented in teleconferences. The most common reasons for a decision against tPA treatment were the fact that the time window was exceeded before unclear onset of symptoms or visible hypodensity in CT scans, was 15 minutes (mean 15.6 minutes, SD 8.2 minutes).

On the basis of the total number of 4178 stroke patients (which included ischemic and hemorrhagic strokes) who were admitted to the participating local hospitals in 2003, the 86 patients receiving tPA treatment in the first 12 months from (February 1, 2003, to Jan 31, 2004) represented a rate of 2.1%. While improving the organization of prehospital and in-hospital management, the number of thrombolyses increased from 42 during the first 7 months to 63 in the second period between October 2003 and March 2004 (1 patient in April 2004). According to the information from the 12 local hospitals, only 10 patients had received systemic thrombolysis in the year before TEMPIS was implemented. The Table shows a comparison of the result of the present study with data from previous publications.

Clinical Data
Protocol violations occurred in 15 cases (15%). Four patients had either 3 points (1 patient with complete cortical blindness) or 4 points (3 cases) on the NIHSS, whereas 6 patients presented with >20 NIHSS points (2 with 21 points, 1 with 22, and 3 with 23). In 5 cases, administration of tPA was started later than 3 hours from symptom onset (but all within 3 hours and 15 minutes). Mean time to thrombolysis was 141 minutes. The percentage of patients treated within 90 minutes from onset was only 5%. Symptomatic hemorrhage occurred in 1 patient with protocol violations, and 2 patients died. No increase in the complication rate was observed in patients with >20 points on the NIHSS or a delayed start of treatment. With very small numbers, this difference was not statistically significant. In-hospital mortality was 10.4%, and the average (median) in-hospital stay was 12 days.

Cerebral Hemorrhages
Follow-up CT-scans were performed after a median of 21 hours after administration of tPA. In 2 cases, an MRI scan was done instead of a CT scan because a brainstem infarct was suspected. In 1 of these MRI scans, which included gradient-recalled echo imaging, a secondary hemorrhage was revealed. In 27 patients (25%), hemorrhages were detected on the follow-up CT scans. For 3 patients, the follow-up CT scans were not accessible. In these cases, assessments by the local radiologists were used for the evaluation.

According to the described criteria, the hemorrhages were categorized as HI 1 (n=2), HI2 (n=11), PH1 (n=4), PH2 (n=7), and focal subarachnoid hemorrhages (n=3). Nine patients had a symptomatic hemorrhage within 36 hours, 3 of them with small bleeds (1 with HI1 and 2 with HI2) but space-occupying infarcts and clinical deterioration. Three patients had deterioration and hemorrhagic complications

### Table: Comparison of Present Study With Previous Publications

<table>
<thead>
<tr>
<th></th>
<th>TEMPIS</th>
<th>NINDS²</th>
<th>Cologne Experience¹⁸</th>
<th>Cleveland Experience⁶</th>
<th>Hospitals With ≤5 Thrombolyses per Year²</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>106</td>
<td>312</td>
<td>100</td>
<td>70</td>
<td>58</td>
</tr>
<tr>
<td>Age (mean), y</td>
<td>68</td>
<td>67</td>
<td>63</td>
<td>69</td>
<td>64.1*</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>41</td>
<td>43</td>
<td>40</td>
<td>51</td>
<td>44.4*</td>
</tr>
<tr>
<td>Median NIHSS score (range)</td>
<td>13 (2–23)</td>
<td>14 (1–37)</td>
<td>12 (2–37)</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Symptomatic hemorrhage, %</td>
<td>8.5</td>
<td>6.4 (P=0.5)</td>
<td>5.0 (P=0.3)</td>
<td>15.7 (P=0.1)</td>
<td>Not reported</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>10.4</td>
<td>Not reported</td>
<td>Not reported</td>
<td>15.7 (P=0.3)</td>
<td>24.1 (P=0.02)</td>
</tr>
<tr>
<td>Mortality within 7 days, %</td>
<td>5.7</td>
<td>5</td>
<td>8</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Onset to admission mean, min</td>
<td>65±25</td>
<td>Not reported</td>
<td>78</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Mean door-to-needle time, min</td>
<td>76±24</td>
<td>Not reported</td>
<td>48±25</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Mean time to treatment, min</td>
<td>141±27</td>
<td>Not reported</td>
<td>124</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Percentage of tPA administered within 90 min</td>
<td>5</td>
<td>48</td>
<td>26</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data of the entire cohort of patients with tPA treatment in German Stroke Registers Study Group (ADSR) in 2000. The data of the subgroup in hospitals with ≤5 systemic thrombolyses were not reported. The symptomatic hemorrhage rate and in-hospital mortality rate were compared with the TEMPIS results.
later than 48 hours after thrombolysis, 1 of them with PH2 and the other patients with H12. Three of the PH1-bleeds and 1 PH2 hemorrhage (small clot located in the cerebellum remote from the infarcted area) were observed without clinical deterioration.

Discussion
This is the first analysis of a substantial number of thrombolyses in stroke conducted after telemedic evaluation. Only small samples of between 2 and 5 thrombolyses have been reported so far. Previous studies demonstrated that remote evaluation of the CTS and of clinical neurological status with the NIHSS could be performed with high reliability and validity.

The present analysis demonstrates that systemic tPA thrombolysis can be administered safely in general hospitals if indicated via teleconsultation by experienced stroke neurologists. Our results show that the rate of symptomatic hemorrhage is comparable to the death rate reported for hospitals experiencing clinical deterioration.

The percentage of patients receiving tPA treatment in the first 12 months of the ongoing project (2.1%) was still lower than the rates reported in established stroke units, but the increasing numbers in the later 7 months indicate a clear improvement. This improvement is related to increased public awareness and better prehospital stroke management achieved by the continuous educational activities of the regional hospitals.

When we focus on the different time segments, it is noteworthy that the onset to admission time is relatively short, but the in-hospital procedures are still too time-consuming. Whereas the time needed for the teleconsultation appears to be adequate, the latencies between admission and CT diagnostics and between teleconsultation and start of tPA infusion need to be reduced. By implementing these measures, more patients could receive tPA. Earlier administration of tPA would provide greater benefit, as shown in the recently published analysis of the pooled data of the tPA stroke trials.

Effective “telethrombolysis” in stroke requires a 24-hour, on-demand teleconsultation service equipped with experienced stroke experts. In TEMPSiS, the expenses for this service amounted to 300 000€ per year. Given the calculated savings of between $3800 and $5000 (3200€ to 4200€) per thrombolysis, the absolute increase of 76 tPA treatments within 1 year would produce a reduction of subsequent costs between 243 200€ and 319 200€. After subtraction of the teleconsultation expenses, the net expenses varied between 56 800€ and −19 200€ per year. This means that the teleconsultation service is cost-effective only with regard to the consultations for possible thrombolyses (396 of 2182 teleconsultations within the first 12 months). Other strategies such as implementation of helicopter transport systems are more expensive, and the reported mean symptom onset–to-hospital arrival time of 135 minutes by helicopter takes longer than in the present analysis.

Considering the increased chance for independence in daily life and better quality of life for the patient, telethrombolysis offers an important therapeutic advance for stroke victims in rural areas. It is cost-efficient and time-saving. Telemedicine should therefore be used to extend the use of systemic thrombolysis. With the integrative concept of TEMPSiS, this approach yields a safe and efficient tPA administration.

Appendix
Participants in the TEMPSiS Group
Stroke neurologists in the stroke centers: S. Ebeling, MD, M. Wimmer, MD, C.M. Hauchwitz, MD (both Munich Harlaching); A. Fürst, MD, B. Ziemus, MD, F. Schlachetzki, MD, and P. Erban, MD (all Regensburg). In the collaborating hospitals: H.U. Kain, MD, R. Hahn, MD (both Mühldorf); C. Metz, MD, S. Hofer, MD (both Freising); R. Haberl, MD, C. Wiedemann, MD (both Pasing); J. Jehle, MD (Straubing); C. Lechner, MD (Dachau); H. Lohner, MD (Rosenheim); F.J. Riedhammer, MD (Burglengenfeld); W. Rothenberger, MD (Bad Tölz); U. Schulten-Baumer, MD (Eggenfelden); H. Schneider, MD, B. Nimnrüchter, MD, K. Pürner, MD (Ebersberg); K.F. Seidl, MD (Kelheim); and H. Zahnweh, MD (Cham).

Acknowledgments
TEMPSiS is supported by the Bavarian health insurance companies; Bavarian State Ministry for Employment and Social Order, Family and Women; and the German Stroke Foundation. Boehringer Ingelheim Pharma GmbH & Co KG supports the project by dispensing the stroke code boxes in all participating hospitals.

References


Telemedicine for Safe and Extended Use of Thrombolysis in Stroke: The Telemedic Pilot Project for Integrative Stroke Care (TEMPiS) in Bavaria

Heinrich J. Audebert, Christian Kukla, Stephan Clarmann von Claranau, Johannes Kühn, Bijan Vatankhah, Johannes Schenkel, Guntram W. Ickenstein, Roman L. Haberl and Markus Horn on behalf of the TEMPiS Group

_Stroke_. 2005;36:287-291; originally published online December 29, 2004; doi: 10.1161/01.STR.0000153015.57892.66

_Stroke_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/36/2/287

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Stroke_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Stroke_ is online at:
http://stroke.ahajournals.org//subscriptions/