Telemedicine for Safe and Extended Use of Thrombolysis in Stroke

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

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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%.1–4

The major reason patients do not receive intravenous thrombolytic therapy is arrival at a stroke treatment center after the 3-hour time window.5 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.6 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.”7

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 hematomas, 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-
“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.

Intermediate analysis for safety assessment was per-
formed 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 com-
pared with historical controls with the χ² test.

**Results**

Between February 1, 2003, and April 7, 2004, a total of 106
patients received systemic thrombolysis through telemedicine
assessment. Data for 356 patients with a possible indication
for thrombolysis were presented in teleconsultations. The most
common reasons for a decision against tPA treatment were
unclear onset of symptoms or visible hypodensity in CT
(n=43), the fact that the time window was exceeded before
the teleconsultation took place (n=23), severe clinical syn-
dromes (n=54), mild clinical deficits or rapid symptom
regression (n=78), suspected epileptic origin (n=14), pre-
treatment with anticoagulation (n=7), and severe concomi-
tant illnesses (n=9). Ten patients became ineligible because
the time window was exceeded during the teleconsultation.
Median duration of the teleconsultation, including transmission
of 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 in-
creased 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 blind-
ness) 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=1), 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

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*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 H2. 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 telethrombolyses have been reported so far.10,11 Previous studies demonstrated that remote evaluation of the CTS12 and of clinical neurological status with the NIHSS13–15 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 in thrombolysis (9.4%)2 but is much lower than the rates reported in inexperienced regional hospitals.2,6 In a recently published meta-analysis, the overall percentage of symptomatic hemorrhages in 15 open-label studies was 5.2%. However, in many of these reports,14,16–18 symptomatic hemorrhage was not clearly defined according to the NINDS criteria19 as was done in the present study. In 1 study, differentiation of hemorrhages was determined according to the judgment of the treating physicians,16 and in other reports, symptomatic hemorrhage was only classified if parenchymal hemorrhages (PH1 and PH2) were seen.17,19 With this latter definition, the symptomatic hemorrhage rate in the present sample would be 5.7%. According to the analysis by Fiorelli et al.,9 hemorrhagic transformations without space-occupying effect do not modify the risk of early deterioration.

The percentage of all types of intracranial hemorrhages ranged between the rates reported in the NINDS trial9 (11%) and the ECASS II trial20 (43% in patients with tPA treatment within 3 hours). It might have been slightly higher if follow-up CT scans had been performed not only after 24 hours (as per protocol) but also routinely after 48 or 72 hours, as was done in ECASS II.

In-hospital mortality remained low, although the mean age of the present sample was relatively high. This mortality rate is comparable to the death rate reported for hospitals experiencing in thrombolysis (9.4%)2 but is much lower than published mortality rates in inexperienced, community-based hospitals.2,6,21

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,2,22 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.23

Effective “telethrombolysis” in stroke requires a 24-hour, on-demand teleconsultation service equipped with experienced stroke experts. In TEMPiS, the expenses for this service amounted to 300 000€ per year. Given the calculated savings of between $3800 and $5000 (3200€ to 4200€)24–26 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,27 and the reported mean symptom onset–to-hospital arrival time of 135 minutes by helicopter28 takes longer than in the present analysis.

Considering the increased chance for independence in activities of 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 TEMPiS, this approach yields a safe and efficient tPA administration.

Appendix
Participants in the TEMPiS 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: U. Kain, MD, R. Hahn, MD (both Mühldorf); C. Metz, MD, S. Hofer, MD (both Freising); R. Hubert, 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. Nimmrichter, MD, K. Pürner, MD (Ebersberg); K.F. Seidl, MD (Kelheim); and H. Zahnweh, MD (Cham).

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References


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