Treating Acute Stroke Patients With Intravenous tPA
The OSF Stroke Network Experience

David Z. Wang, DO; Jean A. Rose, MS; Debra S. Honings, RN; Dennis J. Garwacki, MD; Joseph C. Milbrandt, PhD; for the OSF Stroke Team

**Background and Purpose**—Since the FDA approved tissue plasminogen activator (tPA) in 1996 for acute ischemic stroke, few data have been obtained during the postmarketing phase, and applicability in rural hospitals does not exist. We attempt to examine the safety and outcome of intravenous tPA for acute ischemic stroke in the OSF Stroke Network.

**Methods**—Fifty-seven consecutive patients treated with tPA were examined from June 1996 through December 1998. Admission and discharge National Institute of Health Stroke Scales (NIHSS), modified Rankin Scales (MRS), and discharge disposition, as well as intracerebral hemorrhage and mortality rates, were compared.

**Results**—Of 20 network hospitals, 12 had the experience of administering tPA. No statistically significant differences in the variables recorded were observed for patients treated at the community hospitals versus those who received tPA at the tertiary medical center. In 35% of patients, tPA was initiated by an emergency room or primary care physician in consultation with an OSF neurologist. At discharge, 47% of the patients had minimal or no disability (MRS, 0 to 1), 44% had an NIHSS score of 0 or 1, 54% went home, 25% were transferred to in-patient rehabilitation, 12% went to a nursing or skilled-care facility, and 9% died. Intracerebral hemorrhage rate was 9%; 5% were symptomatic.

**Conclusions**—tPA can be administered safely with good outcome at community and rural hospitals. The OSF Stroke Network can serve as a model to assist small community hospitals to set up stroke programs and deliver up-to-date, acute stroke therapies. (Stroke. 2000;31:77-81.)

**Key Words:** stroke, ischemic ■ thrombolysis ■ tissue plasminogen activator

In June 1996, the FDA approved intravenous tissue plasminogen activator (tPA) for the treatment of acute ischemic stroke within 3 hours of onset. This approval was granted in light of the favorable results obtained in the pivotal National Institutes of Neurological Disorders and Stroke (NINDS) tPA trial. Since its approval, it has been estimated that between 1% and 6% of ischemic stroke patients have been treated with tPA, resulting in part from the strict 3-hour time window and reluctance by many treating physicians. Reports on the use of tPA since its approval are scarce.

Chiu and colleagues published safety and feasibility data of tPA therapy in 30 patients in an urban practice in treatment of ischemic stroke in Houston, Tex. Their outcomes were consistent with the NINDS trial, suggesting that tPA was safe and effective. Although these data confirmed the success of acute thrombolytic therapy in urban hospitals where neurologists are readily available, questions still exist as to the applicability and safety of tPA administration for acute ischemic stroke in community and rural hospitals.

OSF (Sisters of the Third Order of Saint Francis) Saint Francis Medical Center (SFMC) took the initiative to organize a regional OSF Stroke Network (SN) in February 1997. The experience of treating 57 acute ischemic stroke patients among the OSF SN hospitals is presented.

**Subjects and Methods**

The OSF SN consists of 20 hospitals (range, 45 to 730 beds) located in 23 central Illinois counties. This network was established for the purpose of assisting community hospitals in the development of comprehensive stroke prevention and treatment programs for an estimated 1.5 million people in central Illinois. Fourteen (70%) of the 20 hospitals are located in towns with populations <20 000. OSF SFMC is a 730-bed tertiary care center with a dedicated stroke unit offering the full spectrum of stroke diagnosis and therapies. OSF SFMC resources also include 2 medical transport helicopters and 2 full-time Life Flight transport teams. OSF SFMC provides 24-hour telephone consultation service for all 20 SN hospitals, and some sites use telemedicine. Each network site has received physician education by a fellowship-trained stroke neurologist, and all sites have several individuals certified on the NIHSS score. NIHSS scores on admission and discharge are being obtained for all patients admitted with stroke-like symptoms.

When a participating hospital receives an acute stroke patient, the local emergency physician, primary care physician, and/or neurologist have the option of consulting 1 of the OSF neurologists on call. If appropriate, the patient was treated with tPA according to the guidelines published by the American Heart Association. Most patients who received tPA among SN hospitals are transferred to...
OSF SFMC. Subsequent transfer of the patient to OSF SFMC is not required. However, transfer is an option if concerns exist about neurosurgery/neurological backup or if access to blood products is needed. The decision to treat with tPA and/or to transfer the patient was made jointly between the local physician and the consulting OSF SFMC neurologist.

Data were collected on 57 consecutive patients treated with intravenous tPA and cared for at OSF SFMC between June 1996 and December 1998. NINDS guidelines for tPA administration for acute ischemic stroke were followed closely. Patients were grouped into 2 categories: those who received tPA at a community hospital and transferred to OSF SFMC and those who were given tPA at OSF SFMC and remained there throughout the course of their acute hospitalization. An OSF neurologist at a non–OSF SN hospital managed 5 patients, and 5 patients were transferred to OSF SFMC from a non–OSF SN hospital. Patients were given 0.9 mg/kg IV tPA (maximum, 90 mg). Ten percent of the total dose was given as bolus; the rest was infused over 60 minutes. Blood pressure was controlled with antihypertensives such as labetalol. In most cases, systolic blood pressure was maintained at \( \leq 185 \) mm Hg, with a diastolic blood pressure \( \leq 110 \) mm Hg.

Demographic information, including age, sex, and pertinent medical history, was obtained from medical records. Variables included onset of symptom time, emergency room arrival time, laboratory draw time, time of CT, time of tPA bolus administration, mortality, and adverse events. Stroke subtype was determined by use of Treatment of Acute Stroke Trial (TOAST) criteria.6 Outcome was evaluated by comparison of baseline and discharge NIH Stroke Scales (NIHSS), modified Rankin Scale (MRS), discharge disposition, mortality, and length of immediate hospitalization. NIHSS scores were done by a certified staff member. Descriptive and frequency statistical analyses were obtained and comparisons were made by use of SPSS for Windows, version 8.0 (SPSS Inc).

**Results**

**Demographics**

Fifty-seven patients were treated with intravenous tPA at 12 SN hospitals and 2 non-SN hospitals between June 1996 and December 1998 (Table 1). During this same period, \( \approx 900 \) ischemic stroke patients were treated at the OSF Comprehen-

<table>
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<tr>
<th>Town</th>
<th>Facility</th>
<th>County</th>
<th>Beds, n</th>
<th>On-Site Neurology</th>
<th>Distance to SFMC, miles</th>
<th>tPA Patients, n</th>
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<td>Peoria</td>
<td>730</td>
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<td>23</td>
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<td>251</td>
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</table>

*Not affiliated with the OSF SN but treated by OSF neurology.

**TABLE 1. Hospitals Used in This Study**

**TABLE 2. Patient Demographics Compared With Chiu et al² and NINDS Trial**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OSF SN (n=57)</th>
<th>Houston (n=30)</th>
<th>NINDS Parts 1/2</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>71 (41–91)*</td>
<td>66 (32–90)*</td>
<td>67/69</td>
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<td>Female sex, n (%)</td>
<td>23 (40)</td>
<td>47</td>
<td>42/44</td>
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<tr>
<td>NIHSS admission</td>
<td>14 (4–25)*</td>
<td>14 (3–36)*</td>
<td>14/14</td>
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<tr>
<td>Hypertension, n (%)</td>
<td>26 (46)</td>
<td>53</td>
<td>66/67</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>16 (28)</td>
<td>30</td>
<td>18/20</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>15 (26)</td>
<td>30</td>
<td>43/27</td>
</tr>
<tr>
<td>Prior stroke, n (%)</td>
<td>8 (14)</td>
<td>13</td>
<td>17/12</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>8 (14)</td>
<td>10</td>
<td>24/21</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>6 (11)</td>
<td>24</td>
<td>25/22</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>5 (9)</td>
<td>20</td>
<td>14/16</td>
</tr>
<tr>
<td>Acute length of stay, d</td>
<td>6 (1–23)*</td>
<td>9</td>
<td>10.9</td>
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<tr>
<td>Carotid disease defined by &gt;50% stenosis, n (%)</td>
<td>11 (19)</td>
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</table>

*Range.
patients (35%) with prior consultation with an OSF SN neurologist.

**Admission**
The average NIHSS score at admission was 14 (range, 4 to 25; median, 15) (Table 2). Thirty patients (53%) were admitted with an MRS of 4 or 5; 24 (42%) had an MRS of 2 or 3; and 3 (5%) had relatively mild symptoms as reflected by an MRS of 1. The mean time from door to CT was 33±20 minutes (range, 10 to 87 minutes), and the average time from door to laboratory was 28±21 minutes (range, 10 to 115 minutes). The mean time from onset to tPA treatment was 148±52 minutes (range, 57 to 360 minutes). Six patients (11%) were treated with tPA within 90 minutes of the onset of stroke symptoms, and 5 (9%) were given tPA beyond the maximum FDA recommended time of 180 minutes (183, 185, 250, 293, and 360 minutes).

**Discharge**
The average length of the hospital stay was 6.2 days (range, 1 to 23 days). Thirty-one patients (54%) were discharged to home, 14 (25%) to in-patient rehabilitation services, and 7 (12%) to a nursing home or skilled-care facility; 5 patients (9%) died. Symptomatic intracranial hemorrhage occurred in 3 patients (5%), and 2 (4%) had CT confirmation of asymptomatic intracerebral hemorrhage. In addition, 3 patients (5%) experienced hematuria, and 1 patient died of pericardial hemorrhagic effusion.

Of the patients treated with tPA, 47% were discharged with no or minimal disability as defined by an MRS of 0 or 1, and 44% had an NIHSS score of 0 or 1 at discharge. Sixty-eight percent had >4 points of improvement on NIHSS at discharge compared with admission scores (Figures 1 and 2). The average discharge NIHSS score was 6.3 (range, 0 to 28); the median was 2.

**OSF SFMC Versus Other Hospitals**
Demographic and outcome data were compared for patients treated with tPA at a community hospital and transferred to OSF SFMC and those who were given tPA at OSF SFMC and remained there throughout the course of their hospitalization. No statistically significant difference in age, time from door to CT or laboratory, or length of stay was observed between the groups (Table 3). NIHSS scores and MRS at admission and discharge were higher for patients given tPA at OSF SFMC, but these differences were not statistically significant. The time from onset of symptoms to tPA administration was shorter at the community hospitals compared with OSF SFMC (mean, 141 versus 155 minutes).

Other than the treatment with tPA beyond the 180-minute window in 5 patients, no other patients were found to have deviated from the protocol. Complication rates for hemorrhage, death, and myocardial infarction (MI) did not appear to differ between patients given tPA at outlying hospitals and those treated at OSF SFMC.

**Discussion**
Between June 1996 and December 1998, ≈900 ischemic stroke patients were treated at the OSF Comprehensive Stroke Center. Of these 900 patients, 57 (6.3%) were treated with tPA. The OSF SN data suggest that nearly half of the 57 patients who received tPA had complete recovery and that tPA appeared to be effective regardless of stroke subtype or severity. Most patients treated with tPA were discharged home (54%). The length of stay in this series was 6.2 days. In general, patients who had a longer length of stay typically...
presented with multiple complications or compounding factors, such as intracerebral hemorrhage, MI, and carotid endarterectomy.

The NINDS trial excluded patients with acute MI; therefore, no correlation between mortality after tPA for acute stroke and MI has been established. In this study, 3 of the 5 patients who died had symptoms consistent with acute MI. One patient developed Dressler’s syndrome (confirmed by echocardiogram) and worsened after tPA treatment. Chiu et al.2 did not exclude these patients and found 2 patients in whom hemopericardium occurred after tPA administration. Taken together, intravenous tPA should be cautiously or perhaps not considered for patients presenting with concomitant stroke and acute or recent MI.

Of the 57 patients, 5 were treated outside the 180-minute window. Inaccurate initial reporting of symptom onset time occurred in 3 of the 5 patients. The other 2 patients were treated at 183 and 185 minutes, and delays occurred in drug administration. Although 5 patients were treated outside the window, no significant complications occurred in any. Of importance, however, is that the degree of clinical improvement was not as pronounced in these patients compared with the other 52.

Complication rates were collected through hospital discharge. The rates of symptomatic (5%) and nonsymptomatic (4%) intracerebral hemorrhage were similar to the results of the NINDS trial (10%), although those data were collected through 3 months.1 Twenty-one patients (37%) had repeated CT scans within 72 hours of tPA treatment. The decision to repeat CT scans was based on the patient’s clinical presentation and the need to consider anticoagulation for secondary stroke prevention. It is important to note that a CT scan was not repeated in every patient, so the rate of nonsymptomatic intracerebral hemorrhage may be underestimated. One patient who died as a result of intraventricular and intracerebral hemorrhage also suffered an acute MI. In another patient, death caused by intracerebral hemorrhage was likely related to prolonged hypertension (systolic blood pressure >190) that persisted for >6 hours. In addition to intracerebral hemorrhages, other hemor-

rhages likely related to tPA treatment observed in this study included hematuria (5 patients) and mild to moderate bruising of the skin. Complication rates were not significantly different between patients treated at outlying hospitals and those treated at OSF SFMC. This finding should be cautiously interpreted because of the relatively low number of patients in this series.

One of the primary goals of establishing the OSF SN was to provide access to neurological expertise in rural and community hospitals. This need has been more urgent since the approval of tPA for acute ischemic stroke. Twenty of 57 patients were treated with tPA at facilities without on-site neurological expertise, and either an emergency room or primary care physician initiated the treatment. Most of these patients were given tPA after telephone consultation with an OSF SN neurologist. Once tPA was initiated, these patients were transported by helicopter to OSF SFMC. Transfer, in most cases, was requested because of a lack of neurosurgical backup and/or 24-hour availability of blood products at the outlying community hospitals.

Even with the growing evidence supporting the use of thrombolytics for acute ischemic stroke, many physicians, including some neurologists, are still skeptical and will rarely or never use tPA. This study demonstrated that tPA can be safely given to acute ischemic stroke patients in rural and community hospitals with or without on-site neurology. In addition, patients receiving tPA at smaller community hospitals will have a fairly high potential for a good outcome. The present findings suggest that in smaller rural hospitals, the times from the door to CT and the door to the laboratory can be within or shorter than the NINDS consensus guideline for stroke workups.10–12 This fact is quite impressive and suggests that regardless of hospital size, a system to do expedited stroke workups can be set up and successfully implemented by a stroke team. Another important factor to successfully administer tPA is strict adherence to the NINDS protocol and AHA treatment guidelines.7,10–13

tPA can be safely and effectively given with good outcome in patients with acute ischemic stroke who present at rural community hospitals. In such facilities, it is very likely that these patients will be under the direct care of emergency and/or primary care physicians. To assist physicians in these cases, community hospitals and its physicians must have access to 24-hour neuroscience support. Such neuroscience backup will come only from larger regional medical centers. These regional centers should also assist with or provide community hospitals with physician education and address their concerns regarding thrombolytic therapy. Ultimately, such programs will provide the opportunity for patients to receive stroke therapies previously unavailable to patients in those rural areas.

Appendix

The OSF stroke team participants were Angela Benavides, MD; Chester R. Dela Cruz, MD; André Durocher, MD; Edward Hui, MD, PhD; Maria Karbowska-Jankowska, MD; Jorge C. Kattah, MD; Jai Kumar, MD; John McLean, MD; Richard Miller, MD; Michelle Roda, DO; and Pamela J. Tolson, BSN.

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References


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