WISCONSIN MEDICAL JOURNAL

Administration of Tissue Plasminogen Activator for Acute Ischemic Stroke in a Rural Wisconsin Hospital

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ABSTRACT

Background: Tissue plasminogen activator (tPA) has provided a means to improve functional outcome of patients in the treatment of acute ischemic stroke.

Methods: A retrospective chart analysis of ischemic stroke patients presenting from January 1995 to April 2007 to a particular hospital emergency department located in Ladysmith, Wis was conducted. The following factors were analyzed: door-to-tPA time, National Institutes of Health Stroke Scores (NIHSS) at admission and discharge, complication rates, disposition status, contraindications for receiving tPA, and specialties of physicians involved with stroke care.

Results: During this time period, data was available for 108 patients diagnosed with ischemic stroke treated by physicians in 3 specialties (family practice, internal medicine, and emergency medicine). Of these patients, 18 were treated with tPA for an overall tPA administration rate of 16.2%. Onset of symptoms >3 hours prior to presentation was the most common contraindication to tPA administration. Door-to-tPA time was <60 minutes in 38.9% of cases. Patients treated with tPA were more likely to be discharged home and were less likely to expire within the following month; however, these differences did not reach statistical significance.

Conclusions: This study provides evidence that tPA can be safely administered in rural hospitals. Physicians working in rural emergency departments are able to diagnose and manage acute ischemic stroke within the guidelines established by the National Institute of Neurologic Disorders and Stroke (NINDS) without increased complication rates. Making tPA available in rural communities increases access to treatment and improves outcomes of patients with acute ischemic stroke.

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INTRODUCTION

Acute ischemic stroke affects over 500,000 Americans each year.[1] In Wisconsin alone, over 81,000 individuals have suffered from stroke.[2] Annually in Wisconsin, 14,000 patients are discharged from hospitals with the diagnosis of stroke, and 3400 patients die; the majority of these strokes are ischemic in etiology.[2] The introduction of tissue plasminogen activator (tPA) for the treatment of acute ischemic stroke is a way to improve functional outcome of these patients.[3] Although initial clinical trials of tPA were conducted at larger university hospitals, subsequent trials have shown that tPA can be used in community hospitals with similar results.[4-6] Our study varies from previous studies in the resources available for the treatment of ischemic stroke as outlined below.

The hospital in this study is a 41-bed acute care hospital located in northwestern Wisconsin. The hospital's emergency department sees approximately 15 acute ischemic stroke cases annually. A standard ischemic stroke and tPA administration protocol was introduced in 1995. Family practice, internal medicine, and emergency department physicians staff the emergency department. Twenty-four hour computed tomography (CT) is available. CT images are read via teleradiology in Eau Claire, Wis, which is approximately 60 miles away. Neurologists are not on staff at the hospital in this study; however, consultation is available via telecommunication with neurologists in Eau Claire and Marshfield, Wis. The nearest neurosurgeons are located in Eau Claire.

Through our chart analysis, we sought to show that tPA has been successfully and safely administered in a rural hospital staffed by physicians in a variety of subspecialties where an acute ischemic stroke and tPA

administration protocol is in place. The availability of 24-hour CT scanners, teleradiology, and telecommunication makes local treatment of acute ischemic stroke possible for rural communities who have staff radiologists or neurologists available on a limited basis. Given the need to administer tPA within 3 hours of onset of symptoms, many individuals located in rural areas would not have access to tPA unless it is provided by smaller hospitals. In this retrospective analysis, we sought to analyze the efficacy of tPA administered in a rural Wisconsin hospital.

In addition to assessing the efficacy of administration of tPA at this hospital, we also sought to assess the limitations for the administration of tPA. Previous studies have documented rates of tPA administration of <5%.[7] By looking at the amount of time between when the patient walked through the door to when tPA was administered (door-to-tPA times) and contraindications cited in patients not receiving tPA for acute ischemic stroke, we sought to assess improvements that could be made at our institution and in the community for the treatment of acute ischemic stroke.

METHODS

A retrospective chart analysis of ischemic stroke patients presenting from January 1995 to April 2007 to a particular hospital emergency department located in Ladysmith, Wis was conducted. During these years, a tPA protocol was established and utilized. Charts with the following ICD-9 codes were analyzed: 434.00 (cerebral thrombosis without mention of cerebral infarction), 434.01 (cerebral thrombosis with cerebral infarction), 434.10 (cerebral embolism without mention of cerebral infarction), 434.11 (cerebral embolism with cerebral infarction), 434.90 (cerebral artery occlusion without mention of cerebral infarction), 434.91 (cerebral artery occlusion with cerebral infarction), 997.02 (iatrogenic cerebrovascular infarction or hemorrhage), E934.4 (adverse effects of fibrinolysis-affecting drugs), and 436 (acute but ill-defined cerebrovascular disease). This study included charts that pertained only to those presenting to the emergency department for the initial evaluation and treatment of stroke regardless of time of onset. All patients' CT scans were read by teleradiology. For patients who received tPA, we assessed the following factors: door-to-tPA time, NIHSS at admission and at discharge, complications from tPA, and disposition status of patients receiving tPA. For patients presenting with ischemic stroke who did not receive tPA, we examined NIHSS at admission and at discharge, contraindications for receiving tPA, and disposition status. The specialties of physicians involved with stroke care and the frequency of use of neurology consultation was also examined for all cases.

Table 1. Demographics

	tPA	Non-tPA	*P*-value
N	18	90	–
Age (mean±SD)	71.6±11.3	77.1±12.1	0.0819
Male (%)	61.1	51.5	0.6060

N=number of patients.

Descriptive statistics, including percentages, means, standard deviations (SD), and standard errors (SE), were computed for the following outcomes: demographics, door-to-tPA time, NIHSS, disposition, tPA administration, complications, and inpatient mortality. In addition, Chi-square or Fisher's exact test was used to evaluate the differences in gender and disposition between tPA and non-tPA groups. A 2-sample t-test was used to compare age and NIHSS at admission between the 2 groups, while a matched-sample t-test was applied to analyze the change in NIHSS for the tPA group from admission to discharge. Complication rates and inpatient mortality rates were compared to those rates documented by Hess et al using Fisher's exact test, and a 95% confidence interval (CI) was calculated for overall rate of tPA administration. All statistical analyses were performed using SAS version 9.1.

RESULTS

Demographics

Data was available for 18 patients in the tPA group and 90 patients in the non-tPA group (Table 1). In the tPA group, 61% of patients were male (39% female), and 51.5% of the patients in the non-tPA group were male (48.5% female). The difference between the groups was not statistically significant (P=0.60). The mean age of the tPA group was 71.6±11.3 years, and the mean age for the non-tPA group was 77.1±12.1 years. This difference was not statistically significant (P=0.08).

The most common contraindication to the use of tPA was onset of symptoms >3 hours prior to presentation to the emergency department (Figure 1). In addition, unknown time of symptom onset and an International Normalized Ratio (INR) or prothrombin time (PT) >1.5 accounted for 73.8% of contraindications cited.

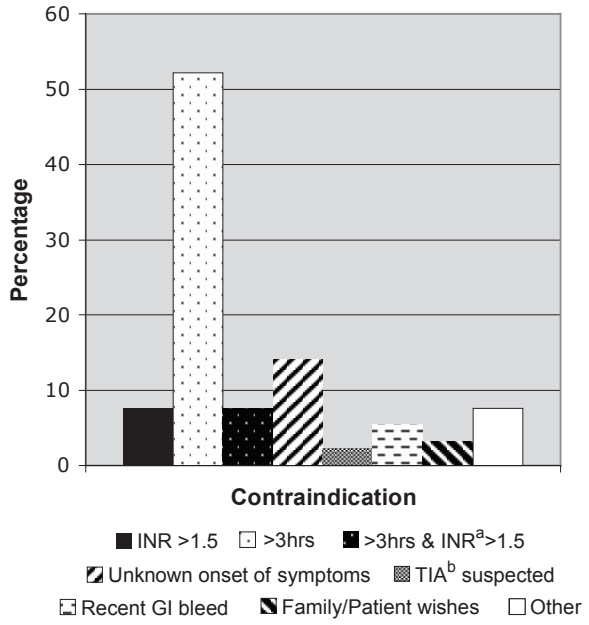

Figure 1. Contraindications for tissue plasminogen activator (tPA) use cited by physicians.
[a] International Normalized Ratio
[b] Transient ischemic attack

Door-to-tPA Time
Mean door-to-tPA time was 79.2±6.7 (mean+SE) minutes. There were 38.9% (7 of 18) with door-to-tPA time of <60 minutes.

NIHSS
At both admission and discharge, 6 patients in the tPA group received NIHSS. The mean NIHSS at admission was 12.83±2.48 (mean+SE), and the mean NIHSS at discharge was 7.33±2.62. This difference is statistically significant (P=0.02).

NIHSS at admission was available for 14 of 18 patients in the tPA group (mean±SE=15.07±2.14), and available for 18 of 96 patients in the non-tPA group (mean±SE=11.22±2.11). The difference in NIHSS at admission between the 2 groups was not significant (P=0.22).

Disposition
Patients receiving tPA had higher rates of discharge to home, transfer to swing beds, and transfer to other facilities than patients not receiving tPA. Fewer patients in the tPA group expired (mortality related to the patient's recent stroke) within 1 month than in the non-tPA group (Figure 2). However, contingency table analysis using Fisher's exact test did not reveal these differences to be significant (P=0.1225).

Specialty of Physicians Treating Ischemic Stroke Patients in the Emergency Department
Physicians representing 3 specialties (family practice, emergency medicine, internal medicine) evaluated ischemic stroke patients in the emergency department during the study period. Of these physicians (28 total), 11 administered tPA. A total of 111 patient charts were available for review, and the proportion of patients assessed and treated with tPA by specialty are as follows: family practice physicians assessed 42 patients and treated 7 (16.7%) with tPA, internal medicine physicians assessed 42 patients and treated 7 (16.7%) with tPA, and emergency department physicians assessed 27 and treated 4 (14.8%) patients with tPA (Figure 3, Table 2). An overall rate of tPA administration was 16.2% (18/111; 95% confidence interval=9.3%, 23.1%), which was significantly higher than other documented rates of 1.6-6.3% (P<0.05).[5-6,8]

Complication Rates
The complication rate of intracerebral bleed for the tPA group was 5.2% (1/19). Using Fisher's exact test, this rate is not significantly different from the documented rates of 0.0% (0/30) reported by Hess et al (P=0.375).[4] This patient had symptoms present for over 3 hours, and tPA was administered after the increased risk of hemorrhage was explained to family members and informed consent was signed. The patient developed cerebral hemorrhage and died.

Inpatient Mortality
As mentioned previously, 1 patient who received tPA died prior to discharge from the hospital. The inpatient mortality rate of 5.3% (1/19) for the tPA group was not significantly different from the 7% rate documented by Hess et al (P=1.000).[4]

DISCUSSION

The administration rate of tPA (16.2%) at this rural Wisconsin hospital was higher than other previously documented rates. Studies in other rural communities have documented rates of 1.6-6.3%.[5-6,8] The comprehensive training provided to the physicians and staff at this hospital regarding acute stroke management and tPA administration may explain the higher rates of tPA administration. All physicians employed at this hospital emergency department are required to successfully complete training on the tPA protocol, including the stroke management training components established by the American Heart Association Advanced Cardiac Life Support Courses and the American Stroke Association's NIHSS Course.[9]

For the patients in this study, the average door-to-tPA time approached the 60-minute guideline. Other rural medical facilities have also documented door-to-

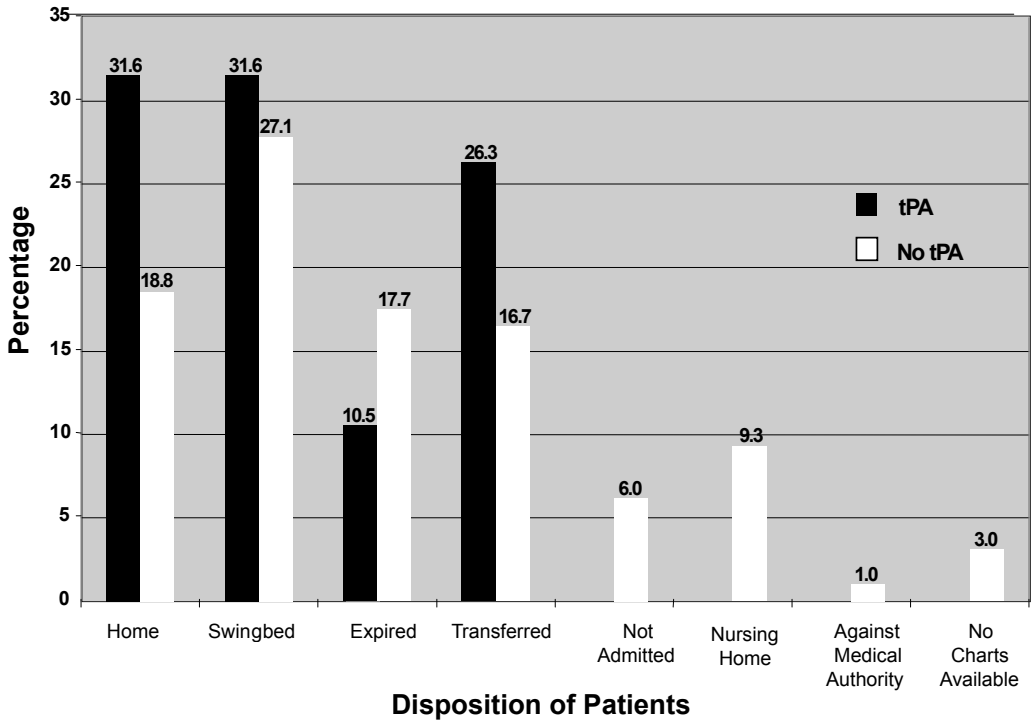

Figure 2. Disposition of patients treated with tissue plasminogen activator (tPA) versus no tPA for acute ischemic stroke.

tPA times comparable to this hospital.[6,8] These results indicate that the evaluation of stroke by physicians in rural communities can be achieved within a timeframe similar to other institutions.[7,10-11]

When compared to other published studies on tPA administration in rural communities, the complication rate of intracerebral bleed was not significantly different (5.6%).[4] The only case of intracerebral bleed in our study occurred in a patient receiving tPA outside the optimal window of administration time. Patients in the present study who received tPA within the recommended timelines experienced no intracerebral hemorrhages.

Although patients in our study who received tPA had a higher rate of discharge to home versus patients not receiving tPA, the difference was not statistically significant. This may be due to the small sample size (N=19 patients treated with tPA).

In Wang et al's study, 54% of stroke patients treated with tPA were discharged to home, compared to 31.6% in this study. Given the significant improvements in NIHSS, final disposition to home likely reflects the improvement in disability that is possible after administration of tPA. The NINDS Study Group showed tPA resulted in a 12% increase in the number of patients without disability or with minimal disability.[3] The effects of tPA in decreasing disability in stroke patients accounts for increased rates of discharges to home.

Inpatient mortality of patients treated with tPA was lower than those not treated with tPA. Hess et al documented an inpatient mortality rate of 7% in patients treated with tPA; a rate similar to the 10.5% rate in this study. The NINDS Study Group did not document a mortality advantage in patients treated with tPA.[3] It is possible that the lower rate of inpatient mortality documented in the present study is due to confounding factors. Physicians may be more likely to administer tPA to patients whose NIHSS are lower. The physicians may assume the risk of administration as being greater than the functional improvement to be achieved by tPA in those with higher NIHSS.

Interestingly, patients receiving tPA were more likely to be transferred than those not receiving tPA. The reasons for transfer ranged from desire for rehabilitation at a designated stroke rehabilitation center to management of cardiac issues that developed while an inpatient. No patients were transferred due to complications directly related to tPA administration.

Onset of symptoms of >3 hours prior to presentation to the emergency department was the most common contraindication to tPA administration. Other rural communities treating stroke patients have also cited this as the most common reason tPA cannot be given.[4] Specific barriers to achieving this time goal that are pertinent to patients in rural communities include the time to travel to hospitals, which for some

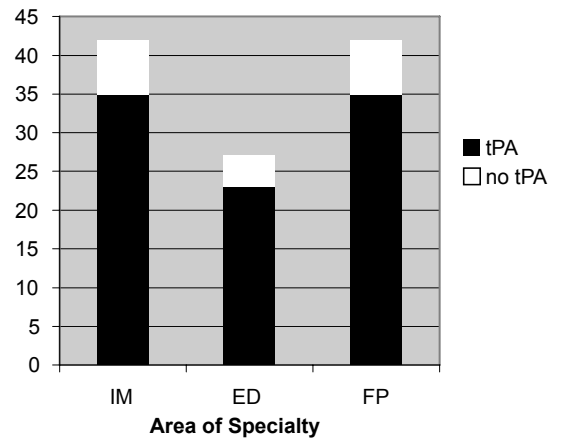

Figure 3. Number of patients assessed and treated with tissue plasminogen activator (tPA) for acute ischemic stroke by specialty. IM=Internal medicine; ED=Emergency department; FP=Family practice.

Table 2. Specialty of Physicians Treating Ischemic Stroke Patients in the Emergency Departments with Either tPA or No tPA

	Internal Medicine	Emergency Department	Family Practice
tPA (N)	7	4	7
Non-tPA (N)	35	23	35
tPA (%)	16.7	14.8	16.7

N=number of patients

individuals in this location may be an hour drive, and public education on symptoms of stroke.

We believe the initial and critical response to acute ischemic stroke care relates to patient education focusing on recognizing the signs and symptoms of stroke and the need for rapid medical care. Patients with acute ischemic stroke should be transferred to medical centers with established acute stroke protocols in order to meet the time guidelines for the potential administration of tPA. Rural emergency medical technicians, first responders, and dispatchers need to be knowledgeable of the signs of acute ischemic stroke and direct patients to health care centers where tPA protocols are established.

We believe that this retrospective study further supports expansion of acute stroke protocols in rural hospitals, so more patients can receive tPA within the recommended time window. By limiting tPA to urban centers, the added burden of reaching a hospital with an established tPA protocol within 3 hours of an onset of symptoms is placed on either the patient or the emergency medical response teams in rural communities. Furthermore, given the data that indicates that the number 1 contraindication for tPA administration is symptom onset of >3 hours, the problem of meeting time guidelines may be compounded if tPA is limited to urban centers.

This study, as well as others, has provided additional evidence that tPA may be safely administered in rural hospitals. Physicians working in rural emergency departments are able to diagnose and manage acute ischemic stroke within the guidelines established by NINDS without increased complication rates. By making tPA available in rural communities, access to treatment is increased and the outcomes of patients with acute ischemic stroke will improve.

Acknowledgments/Funding/Support: Thanks to Marshfield Clinic Research Foundation for providing assistance in the preparation of this manuscript through the services of Linda Weis, Alice Stargardt, and Jennifer Hayes. In addition, thanks to the nursing, radiology, and Emergency Department staff at Rusk County Memorial Hospital and the Edwards Radiology Group of Eau Claire, Wis.
Financial Disclosures: None declared.

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