

Using tPA for acute stroke in a rural setting

Lorraine L. Edwards, MD

Abstract—Controversy continues regarding the safety and efficacy of tissue plasminogen activator (tPA) for stroke outside major centers. We reviewed charts from 1998 to 2004 of 493 patients admitted with TIA or stroke to our small rural hospital. There was a 4% tPA treatment rate with no symptomatic intracranial hemorrhage and zero mortality. IV tPA can be safe and effective in the treatment of acute stroke despite the size of the institution.

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The National Institute of Neurological Disorders and Stroke published a study using IV tissue plasminogen activator (tPA) in 1995, concluding that tPA improved clinical outcomes at 3 months despite an increased incidence of intracerebral hemorrhage.¹ The safety and efficacy of tPA administration outside the setting of a tertiary medical center have been questioned.^{2–4} Most studies outside tertiary medical centers have evaluated mortality and the occurrence of complications such as intracerebral hemorrhage in patient populations of large urban hospitals^{3–6}; similar information from small rural hospitals is sparse.

Mary Lanning Memorial Hospital is a 100-adult bed hospital in Hastings, situated in a rural part of central Nebraska, with a population of 25,000. It serves a wide network of smaller rural communities within a 50-mi radius with a catchment population of approximately 50,000. A Stroke Protocol developed following NIH Guidelines was initiated in 1998. A standard order set and pathway, tPA contraindication checklist, and an approach similar to a Stroke Code were utilized. Emergency department (ED) physicians were responsible for identifying those patients arriving within the treatment window. Neurosurgical support was provided by a larger center within 85 mi.

Methods. We reviewed charts for all patients admitted through the ED with the International Classification of Diseases (9th ed.; ICD 9) diagnosis of stroke or TIA. The number and percentage of patients who presented within the 3-hour window for IV tPA, the time since onset of symptoms, and time to tPA administration were assessed. The occurrence of intracranial hemorrhage and in-hospital mortality along with disposition were identified.

Results. We reviewed 493 cases from 1998 through 2004. These were identified by the ICD 9 code used in the ED. Several patients were seen for multiple events during

those years. One-third of patients (n = 169) arrived within the 3-hour treatment window, and 62% of those received evaluation by a neurologist while in the ED. Forty-seven patients had resolution of symptoms while in the ED and were diagnosed with TIA. Nineteen patients (13% of those in the window excluding patients with TIA) received tPA, an overall treatment rate of 4% (figure 1). Sixteen of the tPA patients were evaluated by a neurologist, one by an internist and two by a family practice physician. The one protocol violation (tPA administered at 262 minutes) occurred with the patient seen by a family practice physician; however, no complications were noted. tPA was not given in 66% (n = 322) of cases owing to arriving outside the treatment window. In the treatment window group, 29% (n = 48) were on therapeutic warfarin (international normalized ratio >1.5), 29% (n = 47) had resolution of symptoms while in the ED, 6% (n = 3) presented with intracranial hemorrhage, and 3% (n = 2) had major trauma at the time stroke. The presence of other tPA contraindications (excessive hyperglycemia, recent major surgery or gastrointestinal bleed, and malignant hypertension) was identified in 32%. Eight patients had multiple exclusionary criteria.

We found that 11 candidates for tPA (6.5%) did not receive the medication owing to late neurology consults or misdiagnosis. Misdiagnosis included visual disturbance secondary to ocular problems (occipital infarct), migraine with neurologic symptoms, and chest pain as focus of care. These patients were in the ED throughout the diagnostic process, and stroke was not recognized until well past the treatment window. Another candidate had an hemoglobin level of 7.9 mg/dL without active blood loss, and subsequently a cardiac thrombus was identified. Four cases with NIH Stroke Scale score of less than 4 were considered too minor by the neurologist to receive tPA. One had multiple embolic events and positive prothrombin gene, and another had an ejection fraction of 10%. Of these 11 patients, 9 were discharged home and 2 to a rehabilitation facility.

Commentary, see page 247

From Central Nebraska Neurology, Hastings, NE.

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Address correspondence and reprint requests to Dr. Lorraine L. Edwards, Central Nebraska Neurology, 2727 W. 2nd Street, Suite 340, Hastings, NE 68901; e-mail: centralnn@alltel.net

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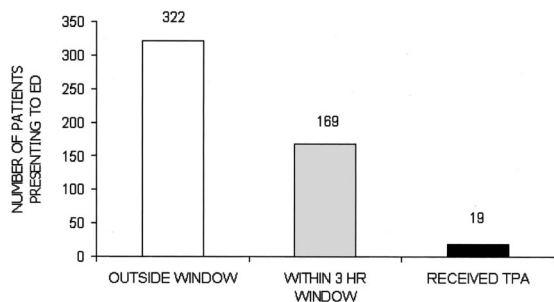


Figure 1. Number of patients presenting to the emergency department (ED). Thirty-four percent of patients presented to ED within the 3-hour treatment window and 11% of those patients received tissue plasminogen activator.

Average time from admission to tPA administration was 84 minutes (30 to 262 minutes). There was only one protocol violation with administration of the drug at 262 minutes. If we remove that case from the calculation, then average time from admission to tPA was 74 minutes. None of the patients receiving tPA had intracranial hemorrhage, and none died while in the hospital. Eleven were discharged home, and 7 went to a rehabilitation facility. One patient was lost to follow-up owing to being transferred to a tertiary hospital for emergent carotid endarterectomy. Patients admitted from a nursing home and discharged back to the nursing home were counted as returning home. In the nontreatment group, 93 (56%) returned home with 41 (35%) to rehabilitation and 9 (6%) to a nursing home (figure 2). In-hospital mortality was 3% in the nontreatment group.

Discussion. Since tPA was approved for use in 1995, there has been controversy about its role in the treatment of acute stroke.^{2,3,7-9} Some clinicians feel it does not offer a great enough benefit to offset the increased risk of hemorrhage.⁶ Others feel it can make a dramatic difference in outcome in some patients.¹ The question of safety in nontertiary medical centers has been at the center of the debate.^{3,9} The National Institute of Neurological Disorders and Stroke study¹ had symptomatic ICH in 6.4% and in hospital mortality of 13%. The Cleveland⁶ and Connecticut⁹ studies found that higher incidence of protocol violations (50 and 67%, respectively) lead to higher incidence of symptomatic ICH. Our institu-

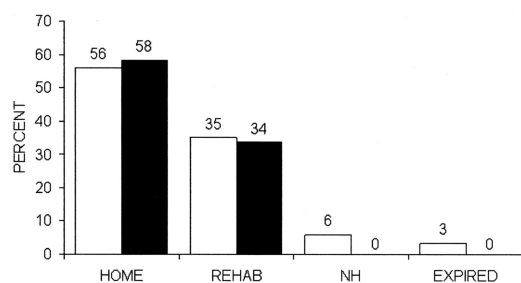


Figure 2. Disposition of patients receiving tissue plasminogen activator (tPA; solid black) and the untreated group (shaded). tPA group sent no patients to the nursing home and had none die. REHAB = subacute or acute rehabilitation facility; NH = nursing home.

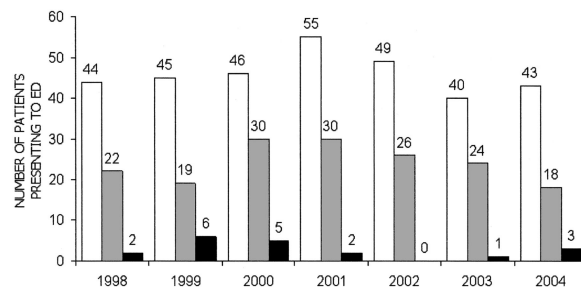


Figure 3. Number of patients presenting to the emergency department (ED) per year. Over the first few years, there was an increase in number of patients reaching the ED within the treatment window and receiving tissue plasminogen activator (tPA). Then those numbers started to fall to preprotocol years. Open bars = presented to ED outside the window; shaded bars = presented within the 3-hour window; black bars = received tPA.

tion does adhere strictly to the exclusionary criteria, and only one major protocol violation was identified. This was a key factor in our lack of symptomatic ICH and zero mortality.

Ours is a study of a fairly small hospital serving a rural community area. The study population had demographics and risk factor profiles similar to other studies.^{1,3-7,9,10} Stroke prevention therapy was in place in 76% of patients (35% on antiplatelet therapy, 21% on warfarin with international normalized ratio >1.5). We have incorporated public education and training of first responders to the need for prompt medical assessment in possible stroke and the importance of arriving quickly at the hospital. This, in combination with our small size, accounts for the high rate of 34% arriving at the ED in a more timely fashion. Twelve percent of patients arriving at the ED missed the window by between 5 and 180 minutes. In another study 11% presented within that same time frame.⁵ These are patients that we should be able to capture into the treatment window with more aggressive education policies. We initially had a pervasive public education program and saw an increase in patients reaching the ED within the treatment window (figure 3). This then decreased over the next couple of years to the initial rate. During those later years, there was staff turnover in the emergency medical technician units, and upon investigation ongoing public education and education of first responders had lapsed. We are now in the process of initiating regularly scheduled training programs and public education messages to try to increase the number of patients reaching the ED within the treatment window.

Our patients who received tPA had a better outcome than those who did not. Compared with other similar studies and the National Institute of Neurological Disorders and Stroke study, our tPA treatment rate was higher (4 vs 1 to 3%). No other study had an intracranial hemorrhage rate of zero. Other studies had mortality rates from 11 to 25%, whereas we had a mortality rate of zero.^{1,3-8} Physicians should

be comfortable administering tPA to appropriate candidates despite the size of their facilities if they have an appropriate protocol and adhere to it.

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NeuroImages

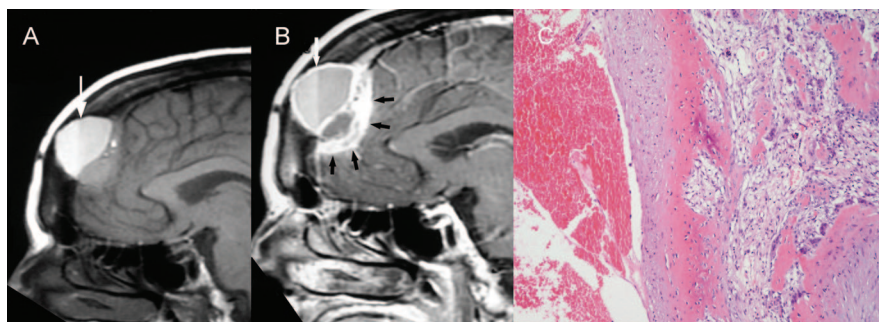


Figure. (A, B) MRI showed a cystic frontal bone lesion with heterogeneous contrast enhancement. (C) Pathologic examination showed an aneurysmal bone cyst.

Aneurysmal frontal bone cyst

A. Torres, MD; J.J. Acebes, PhD; J.A. Narvaez, MD; and S. Boluda, MD, Barcelona, Spain

A 66-year-old woman presented with a 2-month history of headache. Neurologic examination was normal and past history included colonic adenocarcinoma. MRI showed a cystic frontal bone lesion with heterogeneous contrast enhancement (figure, A, B). A preoperative diagnosis of brain metastasis with cranial inva-

sion was made and it was surgically resected. Pathologic examination showed an aneurysmal bone cyst (ABC) (figure, C). The patient recovered with complete resolution of symptoms.

ABCs usually develop in childhood, and long bones are involved in 50% of cases. In 30% of cases, a preexisting condition or history of trauma is present. Skull involvement is rare. There are fewer than 10 cases of frontal ABC described in the literature, all of which have this characteristic radiologic appearance.^{1,2} ABC should be included in the differential of bone neoplasm in this location.

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Address correspondence and reprint requests to Dr. Alberto Torres, Department of Neurosurgery, Hospital de Bellvitge, Barcelona, Spain; e-mail: atorresdiaz72@hotmail.com

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