Direct stroke unit admission of intravenous tissue plasminogen activator: safety, clinical outcome, and hospital cost savings

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Abstract

Background: In the USA, stable intravenous tissue plasminogen activator (IV tPA) patients have traditionally been cared for in an intensive care unit (ICU). We examined the safety of using an acuity-adaptable stroke unit (SU) to manage IV tPA patients.

Methods: We conducted an observational study of consecutive patients admitted to our acuity-adaptable SU over the first 3 years of operation. Safety was assessed by symptomatic intracerebral hemorrhage (sICH) rates, systemic hemorrhage (SH) rates, tPA-related deaths, and transfers from SU to ICU; cost savings and length of stay (LOS) were determined.

Results: We admitted 333 IV tPA patients, of which 302 were admitted directly to the SU. A total of 31 (10%) patients had concurrent systemic hemodynamic or pulmonary compromise warranting direct ICU admission. There were no differences in admission National Institutes of Health Stroke Scale scores between SU and ICU patients (9.0 *versus* 9.5, respectively). Overall sICH rate was 3.3% ($n = 10$) and SH rate was 2.9 ($n = 9$), with no difference between SU and ICU patients. No tPA-related deaths occurred, and no SU patients required transfer to the ICU. Estimated hospital cost savings were US$362,400 for 'avoided' ICU days, and hospital LOS decreased significantly ($p = 0.001$) from 9.8 ± 15.6 days (median 5) in year 1, to 5.2 ± 4.8 days (median 3) by year 3.

Conclusions: IV tPA patients may be safely cared for in a SU when nurses undergo extensive education to ensure clinical competence. Use of the ICU solely for monitoring may constitute significant overuse of system resources at an expense that is not associated with additional safety benefit.

Keywords: stroke units, safety, functional outcome, cost savings

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Introduction

Intravenous tissue plasminogen activator (IV tPA) treatment of ischemic stroke has traditionally required intensive care unit (ICU) admission in the USA to meet ongoing monitoring requirements [Jauch *et al.* 2013; Alberts *et al.* 2011; Singh and Edwards, 2013; Seder and Meyer, 2009; Burns *et al.* 2012]. Concerns for symptomatic intracerebral hemorrhage (sICH), failed recanalization, and evolving malignant symptoms have justified the use of ICU services, although actual ICU needs are usually limited to monitoring/management of blood pressure (BP) and serial neurologic examinations. US stroke units (SUs) vary in capabilities with most comprised simply of designated beds on a nursing unit that admits other types of patients, and US guidelines do not specify SU structure, required nursing knowledge and skills, or staffing. European studies show that SUs are associated with reduced mortality and improved functional independence [Stroke Unit Trialists' Collaboration, 2007; Langhorne *et al.* 2013; Sun *et al.* 2013], and these units, as well as Asian and Australian units, commonly admit IV tPA-treated patients directly.

ICUs were developed as a method to reorganize nursing care, grouping the sickest patients together [McClenahan, 1974; Fairman and Lynaugh, 1998; Morrow *et al.* 2012; Grenvik and Pinsky, 2009].

Contemporary US ICU admission requirements include physiologic instability, high mortality risk, and an expectation for recovery [Morrow *et al.* 2012; Grenvik and Pinsky, 2009], with most patients requiring significant technologic support. In comparison, IV tPA patients are commonly managed with two peripheral IVs, cardiac monitoring, antihypertensive medication(s), and supplemental oxygen. In addition, ICU bed competition often creates the need for unplanned transfers of the 'most stable' patients [Nager and Khanna, 2009; Asplin *et al.* 2006], to make room for IV tPA cases. Collectively, these factors support the need for evolution of the US SU model toward the European paradigm, with capabilities to support IV tPA management. As no US data exist to support a new SU model, we examined safety and clinical outcomes, while estimating the hospital cost savings associated with managing IV tPA-treated patients in a specialty non-ICU setting.

Methods

We conducted a prospective, observational study of IV tPA-treated acute ischemic stroke patients admitted directly to a highly specialized acuity-adaptable SU. Institutional Review Board approval was obtained to analyze prospectively collected registry data on consecutive IV tPA-treated acute ischemic stroke cases admitted during the first 3 years of SU operations (1 January 2009–31 December 2011). Inclusion criteria were IV tPA treatment on-site or at a remote transferring hospital (drip and ship), and direct admission from the Emergency Department to the SU. Cases were excluded if SU transfer occurred beyond the 24 h serial monitoring period for IV tPA, or if sICH was noted on arrival by noncontrast brain computed tomography of a drip and ship patient. A cohort of ICU-admitted IV tPA-treated ischemic stroke patients, who presented during the same time period with significant systemic hemodynamic and/or pulmonary instability, was assembled to compare appropriateness of the ICU *versus* SU triage decision.

Safety measures included tPA-related death, SU patient transfer to ICU, systemic hemorrhage (SH) requiring transfusion, and sICH defined as parenchymal hematoma-type 2 in combination with worsening of four or more points on the National Institutes of Health Stroke Scale (NIHSS) within 36 h of tPA administration. Hospital length of stay (LOS) and discharge modified Rankin Score (mRS) were also analyzed. Hospital cost savings for 'avoided ICU days' were defined as US$1200 per day, representing the actual difference in direct hospital costs between a single day (24 h) SU and ICU admission, while excluding additional monitoring, medication, and other equipment that may be utilized in the care of a stroke patient.

Stroke unit design

We designed and opened a 20-bed SU in January 2009, using an acuity-adaptable, universal-care model [Emaminia *et al.* 2012; Winter *et al.* 2011; Brown and Gallant, 2006], whereby acute stroke patients without systemic hemodynamic or pulmonary compromise would be admitted directly from the Emergency Department and stay in the same SU bed from admission to discharge. Nurse staffing on the SU was designed to flex according to patient needs, so that patients within the first 24 h of IV tPA treatment were managed using a one-nurse to two-patients assignment. As patients improved and monitoring/management needs decreased, staffing assignments also flexed, so that on average nurse staffing on the SU was based on a one-nurse to three-patients assignment. Physician staffing for SU patients included one senior 'attending' vascular neurologist supported by two neurology resident trainees, and four medical students, to manage 17 patients on average. The SU allowed 24/7 family access and was made up of private rooms with sleeper sofas for family, enabling ongoing patient/family education and training to support discharge and transition to the post-acute environment. An advanced-practice neurovascular nurse specialist oversaw all SU nursing care, education, and training, and a nurse manager with expertise in cardiovascular catheterization and emergency care was hired to oversee unit administration. Table 1 lists required nursing competencies for registered nurses on the SU. Access to the internet-based Neurovascular Education and Training in Stroke Management and Acute Reperfusion Therapies (NET SMART)-Junior program was provided to all SU nurses to support ongoing educational needs and attainment of a specialty stroke nursing certification [NET SMART, 2015].

Statistical analyses

Data were entered and analyzed in SPSS version 20. Analysis of variance was used to compare

Table 1. Required nurse competencies on the acuity-adaptable stroke unit.

- Initiation of, and patient monitoring during intravenous alteplase tissue plasminogen activator infusions
- Calling and responding to Code Stroke alerts for suspected patient deterioration or new stroke events
- Basic skills in clinical localization of findings to vascular territories in the brain
- Certification in the National Institutes of Health Stroke Scale
- Certification in the modified Rankin Score
- Cardiac dysrhythmia interpretation
- Advanced cardiac life support certification
- Cardiopulmonary resuscitation certification
- Central venous monitoring
- Arterial line monitoring
- Initiation and titration of intravenous antihypertensive therapy, including nicardipine continuous infusions
- Knowledge and skills in the management of clinical trial patients

differences in age and total hospital LOS for SU patients during the 3-year study period. Independent samples Mann–Whitney U tests were used to compare differences in SU-admitted IV tPA patients *versus* ICU-admitted IV tPA patients for baseline NIHSS score, SH, sICH, and discharge mRS. Hospital cost savings were calculated by multiplying the US$1200 difference between SU and ICU charges for a single day, by the number of patients admitted directly to the SU. Total hospital cost savings were calculated to reflect just one 24 h reduction in utilization of the ICU as would be expected for a stable IV tPA case without actual critical care needs.

Results

The sample consisted of 333 IV tPA cases admitted between 1 January 2009 and 31 December 2011. Of these, 302 were admitted directly to the SU for IV tPA management and monitoring, while 31 (9.3%) were deemed critical and admitted to the neuroscience intensive care unit (NICU) for systemic hemodynamic and/or pulmonary instability. Table 2 describes the SU IV tPA sample and study endpoints for the 3-year study period. Patients admitted to the SU were similar in age and median NIHSS scores throughout the 3-year period, and 58 (19%) were drip and ship transfers.

Over the 3-year period, no deaths were attributed to IV tPA treatment in the sample, and no cases required transfer to the ICU for deterioration or continued management. SH rates were well beneath the 6.4% reported in the National Institute of Neurological Disorders and Stroke (NINDS) rtPA Stroke Study [National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group, 1995], at 2.3%, 4.7%, and 1.9%, respectively for the 3-year period. Rates for sICH were also beneath the NINDS trial's 6.4% rate at 4.7% in 2009 and 2.8% in both 2010 and 2011, with the majority of sICH occurring in drip and ship transfers. The overall drip and ship sICH rate was 12%; no BP protocol violations occurred during the SU stay of these patients, however, emergency medical services transport records lacked consistent documentation of BP to determine if BP parameters were maintained on route to our facility. Figure 1 shows LOS across the 3-year study period demonstrating a statistically significant ($p = 0.001$) decrease from 9.8 ± 15.6 (median 5) days in 2009, to 5.2 ± 4.8 (median 3) days in 2011. Median discharge mRS scores were 3 for SU patients with 71% of patients discharged to either inpatient or outpatient rehabilitation center care. The total estimated cost savings for avoiding 1 ICU day/patient during this 3-year period was US$362,400.

Table 3 compares characteristics and outcomes among SU and NICU-managed IV tPA patients. Median admission NIHSS score, sICH rate, SH rate, and LOS were similar among patients for the 3-year period. However, mRS was significantly lower in the SU cohort with a median of 3, compared with the NICU median of 6 ($p = 0.001$), reflecting appropriate admission triage of the ICU cohort to this higher level of care.

Discussion

Our study documents the safe management of IV tPA-treated patients in an acuity-adaptable, universal care SU with a flexible nurse staffing model

Table 2. Characteristics and outcomes in stroke unit-managed intravenous tissue plasminogen activator patients.

Year	*n* tPA cases ad- mitted (% total)	Mean age (median; range)	Median ad- mission NIHSS (range)	*n* Drip and ship (%)	tPA complications rates	Length of stay (median); discharge mRS (range)	Estimated total cost savings per avoided ICU day
2009	86 (90%)	64 ± 17 (66; 28–95)	10 (0–32)	19 (22%)	• Overall sICH: 4.7% ($n = 4$) • Drip and ship sICH: 2 (10.5%) • SH: 2.3% ($n = 2$) • tPA-related death: 0	LOS: 9.8 ± 15.6 (5); mRS: 4 (0–6)	US$103,200
2010	107 (88%)	65 ± 17 (68; 21–94)	9 (0–23)	13 (12%)	• Overall sICH: 2.8% ($n = 3$) • Drip and ship sICH: 3 (23%) • SH: 4.7% ($n = 5$) • tPA-related death: 0	LOS: 6.4 ± 5.8 (4); mRS: 3 (0–6)	US$128,400
2011	109 (94%)	65 ± 17 (65; 20–99)	7 (0–23)	26 (24%)	• Overall sICH: 2.8% ($n = 3$) • Drip and ship sICH: 2 (7.7%) • SH: 1.9% ($n = 2$) • tPA-related death: 0	LOS: 5.2 ± 4.8 (3); mRS: 3 (0–6)	US$130,800

LOS, length of stay; mRS = modified Rankin Score; SH, systemic hemorrhage; sICH, symptomatic intracerebral hemorrhage; tPA, tissue plasminogen activator.

Table 3. Comparison of stroke unit *versus* intensive care unit-managed intravenous tissue plasminogen activator patients.

Unit	Median admission National Institutes of Health Stroke Scale	*n* Symptomatic intracerebral hemorrhage	*n* Systemic hemorrhage	Length of stay	Median modified rankin Score at discharge
Neuroscience intensive care unit ($n = 31$)	9.5	1 (3.2%)	1 (3.2%)	6.9 ± 9.7 median 3	6
Stroke unit ($n = 302$)	9*	10* (3.3%)	8* (2.6%)	6.9 ± 9.6* median 4	3**

*p = NS. **p = 0.001.

and highly educated, clinically skilled dedicated stroke nurses. Rates of SH and sICH were acceptable, although sICH rate was highest among the drip and ship subgroup admitted to the unit. As there was no evidence of inappropriate patient selection for thrombolysis in the drip and ship cohort, the higher sICH rate may indicate poor BP control during outside hospital management and/or ambulance transfer, given inconsistent BP documentation in both transfer and ambulance records. However, it is doubtful that admission of drip and ship cases to an NICU would have prevented these sICHs from occurring since there was no evidence of BP protocol violations in these patients during their stay in the SU. Our findings also suggest sound admission triage of unstable IV tPA cases with concurrent multisystem impairment to the NICU, as evidenced by the significantly higher discharge mRS scores in this cohort.

We were unable to obtain actual hospitalization costs in our sample, and therefore we conservatively estimated cost savings by using the difference in NICU and SU direct admission costs at US$1200 per 1-ICU day avoided. While obtaining actual costs would have been preferable, we recognize that this information remains inaccessible in most hospitals throughout the world, and

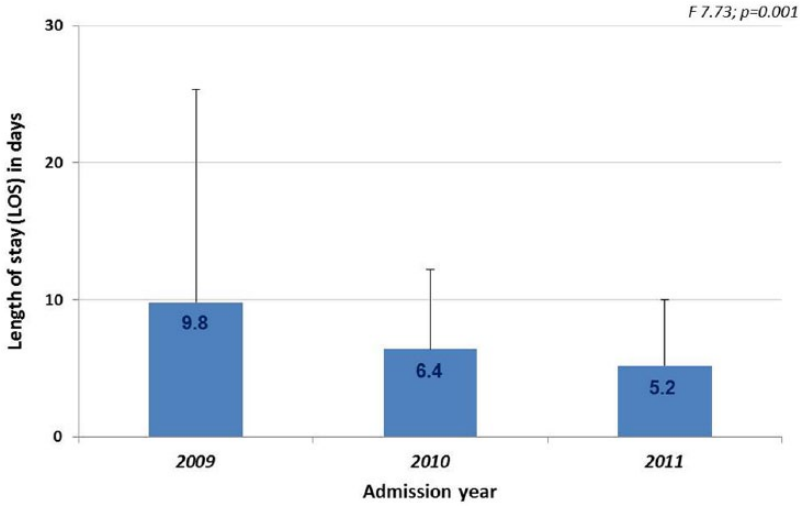

Figure 1. Decline in stroke unit length of stay over time.

therefore our estimation of a US$362,400 savings is likely significantly lower than the true savings incurred. As ICU admission costs commonly have associated routine charges for monitoring, and high acuity nurse staffing and equipment, use of a specialized SU to manage stable IV tPA patients may actually yield a beneficial financial margin, especially given the capitated payment received by many hospitals for acute stroke admissions. In addition, ICUs are best reserved for physiologically unstable patients that require the use of sophisticated technology to prevent death or further deterioration [Morrow *et al.* 2012; Grenvik and Pinsky, 2009; Winter *et al.* 2011], and many hospitals struggle with internal triage to make ICU beds available for specialty patients. We suggest that development of universal-care, acuity-adaptable acute SUs with specialist nurses to oversee care of IV tPA patients offers an opportunity to open ICU beds to more appropriate patients, at no increased risk of suboptimal outcomes. In fact, given the short 6-day average US LOS for acute ischemic stroke patients [CDC, 2015], use of a universal-care acute SU model offers the advantage of maintaining patients within a single care setting under the expert management of specialist stroke nurses for the entire duration of their hospitalization, fostering improved education to patients/family about secondary prevention strategies, and ultimately, better preparation for transition to post-acute settings.

While SUs were among the first interventions shown to reduce mortality and improve functional independence after stroke [Stroke Unit Trialists' Collaboration, 2007; Langhorne *et al.* 2013], work evaluating the impact of SUs has been primarily tied to units that admit patients for significantly longer periods of time, extending well into the post-acute rehabilitative period that does not mirror hospitalization practices in the USA and many other countries. However, in the USA, much work can be done to improve SU care by standardizing recommendations beyond the current limited requirements for 'designated beds' and 8 h of annual continuing education for staff. While our study is limited by its observational methods from assigning a cause-and-effect relationship between patient outcome and the quality of SU services, it nonetheless is a first step towards redirecting US SU services towards a highly specialized paradigm such as that used in Europe. Therefore, we recommend that stroke centers with high IV tPA-treatment volumes explore use of this innovative model to build knowledge of what constitutes SU best practices for these patients in the acute hospital setting.

Conclusion

IV tPA-treated ischemic stroke patients may be safely and cost-effectively managed outside the ICU on acute SUs supported by expert nursing care delivery using an acuity-adaptable, universal-care nurse staffing model. Admission of IV tPA-treated patients to the ICU solely for monitoring may constitute significant overuse of system resources at an expense that may not be justified by safety benefits.

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Conflict of interest statement

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