

Do All Acute Stroke Patients Receiving tPA Require ICU Admission?

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Abstract

Background: Limited resources warrant investigating models for predicting which stroke tissue-type plasminogen activator (tPA) patients benefit from admission to neurologic intensive care unit (neuroICU).

Methods: This model classifies patients who on day 1 of their ICU admission are predicted to receive one or more of 30 subsequent active life supporting treatments. Two groups of patients were compared: low risk monitor (LRM) (patients who did not receive active treatment (AT) on the first day and whose risk of ever receiving active treatment was $\leq 10\%$) and AT (patients who received at least one treatment on any day of their ICU admission).

Results: Compared to LRM group (21 patients), AT group (59 patients) had similar age (75 ± 13 vs. 72 ± 17 , $P = 0.4$), similar gender (male: 56% vs. 52%, $P = 0.8$), similar National Institutes of Health stroke scale (NIHSS, 16 ± 9 vs. 14 ± 8 , $P = 0.4$), and higher Acute Physiologic and Chronic Health Evaluation (APACHE) III scores (62 ± 26 vs. 41 ± 15 , $P = 0.0008$). Compared to LRM group, AT group had longer ICU length of stay (4.5 ± 4.4 vs. 2.5 ± 1.3 , $P = 0.04$), higher ICU mortality (22% vs. 4.7% (one patient DNR/hospice); OR: 5.6; 95% CI: 0.7 - 46.0; $P = 0.1$), and higher hospital mortality (36% vs. 4.7%; OR: 11; 95% CI: 1.4 - 88.0; $P = 0.02$).

Conclusion: The outcome of LRM patients with stroke post-tPA suggests that they may not require admission to a formal neuroICU, improving resource use and reducing costs.

Keywords: Neurologic intensive care unit; Stroke; Ischemic stroke; tPA; Utilization review

Introduction

Recombinant tissue-type plasminogen activator (tPA) was first

approved by the FDA in the United States in 1996 and remains the only medication shown to improve outcomes when given within 3 - 4.5 h after ischemic stroke. Although tPA remains underutilized in patients with acute ischemic stroke, nonetheless, its use is steadily increasing [1]. Patients with acute ischemic stroke who receive tPA are admitted to intensive care unit (ICU) for close monitoring and frequent neurochecks, especially because of risk of major bleeding with tPA.

The concept of resource allocation on the grounds of relative medical benefit is often referred to as triaging: “the process in medicine of finding the most appropriate disposition for a patient based on an assessment of the patient’s illness and its urgency”. A little more than 50 years ago, hospitals opened ICUs with the purpose of caring for the sickest patients, using the newest technology. Today, critical care in the United States costs more than \$80 billion annually [2]. Most of the studies on rationing healthcare and resource allocation regarding ICU admission focused on patients who might be too sick to benefit [3].

In a recent study, the outcome for low risk monitor (LRM) patients suggests they may be treated outside of ICU [4]. That study presented a new model for identifying patients who might be too well to benefit from ICU care. Limited resources, neurointensivists, and neurologic intensive care unit (neuro-ICU) beds warrant investigating models for predicting who will benefit from admission to neuroICU. In this study, we apply the same model to identify patients with ischemic stroke and received intravenous tPA who might not need to be admitted to the neuroICU.

Methods

The Acute Physiologic and Chronic Health Evaluation (APACHE) outcomes database was used to retrospectively identify ischemic stroke patients who received tPA and admitted to our neuroICU between January 2013 and December 2016. Our 16-bed neuroICU is staffed by intensivists (board certified by the American Board of Internal Medicine in Internal Medicine and Critical Care Medicine and certified by the United Council of Neurologic Subspecialties in Neurocritical Care) 24 h/day. The APACHE outcomes database further classifies patients who on day 1 of their neuroICU admission are predicted to receive or not receive one or more of 30 subsequent active life supporting treatments (Table 1). We compared two groups of patients: LRM (patients who did not receive active treatment on the first day and whose risk of ever receiving active treatment was $\leq 10\%$)

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Table 1. Active Life Supporting Treatments

AV pacing	Endoscopies	PA catheter
Barbiturate anesthesia	HFOV	Post-arrest
Cardioversion	Induced hypothermia	Prone positioning
Continuous antiarrhythmic	IABP	Rapid blood transfusion
Continuous arterial drug infusion	IPPV	Reintubation within 24 h
Continuous neuromuscular blockade	IRRT/HD	Vasoactive drug infusion
CRRT	IV replacement excessive fluid loss	Tx of status epilepticus
ECMO	IV vasopressin	VAD
Emergency procedure inside ICU	Intubation in ICU	Vasoactive > one
Emergency procedure outside ICU	NIPPV (BiPAP)	Ventriculostomy

AV: atrioventricular; CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; HFOV: high frequency oscillatory ventilation; IPPV: intermittent positive pressure ventilation; IRRT/HD: intermittent renal replacement therapy/hemodialysis; IV: intravenous; NIPPV (BiPAP): non-invasive positive pressure ventilation (Bilevel positive airway pressure); PA: pulmonary artery; Tx: treatment; VAD: ventricular assist device.

and active treatment (AT) (patients who received at least one of the 30 ICU treatments on any day of their ICU admission). In a previous study [4], data were used to develop and internally and externally validate the APACHE IV risk for active treatment in the ICU. In short, data generated as a result of patient care and recorded in the medical record were collected concurrently or retrospectively for consecutive unselected ICU admissions. Data collected for each patient are shown in Table 2. Detailed descriptions of these demographic, clinical, and physiological items have been previously reported [5, 6].

LRM patients were defined as admissions that did not receive any of the 30 active life supporting treatments listed in Table 1 during their first ICU day. To determine which characteristics influenced risk for AT, a multivariable logistic regression model was developed to estimate the probability that an LRM admission would ever receive AT during the remainder of their ICU stay. The predictor variables in the logistic regression model are listed in Table 2 and were preselected based on previous research [7]. A 10% predicted risk for receiving AT was previously validated as a means for identifying ICU patients with

Table 2. Patient Data Collected and Variables Used for Predicting Risk for Active Treatment Based on Intensive Care Unit Day 1 Data

Age	Continuous measure plus five spline terms
Chronic health variables	Y/N for the following variables: AIDS, hepatic failure, lymphoma, metastatic tumor, immunosuppression, leukemia or myeloma, and cirrhosis. Not used for elective surgery patients.
ICU admission source	Floor, emergency room, operating/recovery room, step down unit, direct admission, other ICU, other hospital, other admission source
ICU admission diagnosis	116 categories, leading to 115 indicator variables ("acute myocardial infarction, other location" is the reference category).
Length of stay before ICU admission	Square root of time in minutes between hospital admission and ICU admission. This is a continuous measure, and four spline terms are added.
Unable to assess Glasgow coma score due to sedation or paralysis	Y/N
Emergency surgery	Y/N
Mechanical ventilation on first ICU day	Y/N
Thrombolytic therapy	Y/N (for patients with acute myocardial infarction)
ICU readmission	Y/N
Glasgow coma score rescaled	15 minus measured Glasgow coma score
PaO ₂ /FiO ₂ ratio rescaled	
APS*	Continuous measure plus five spline terms

*The APS is a sum of weights assigned to 17 physiologic variables. The weights are determined by the most abnormal value for a measurement within first day in intensive care unit. Variables include pulse rate, mean blood pressure, temperature, respiratory rate, PaO₂/FiO₂ ratio (or P(Aa) O₂) for intubated patients with FiO₂ N.5), hematocrit, white blood cell count, creatinine, urine output, blood urea nitrogen, sodium, albumin, bilirubin, glucose, acid base status, and neurological abnormalities based on Glasgow coma score.

Table 3. Baseline Characteristics and Outcomes of the Active Treatment Group and the Low Risk Monitor Group

	Active treatment	LRM	P value
No. of ICU admissions	59	21	
Age (mean ± SD)	75 ± 13	72 ± 17	0.4
APACHE III (mean ± SD)	62 ± 26	41 ± 15	0.0008
Pre-tPA-NIHSS (mean ± SD)	16 ± 9	14 ± 8	0.4
Hospital mortality, n (%)	21 (36)	1 (4.7)	0.006
ICU mortality, n (%)	13 (22)	1 (4.7)	0.07
ICU LOS (mean days ± SD)	4.5 ± 4.4	2.5 ± 1.3	0.04

a low versus a high risk for AT [8]. The 10% threshold gave the highest combination of sensitivity and specificity. This model was validated internally and externally in general ICUs [4]. This study intends to apply this model on ischemic stroke patients who received tPA and admitted to a single center neuroICU.

We excluded patients who had been admitted for less than 4 h, and patients younger than 18 years. Data were entered using a software program that included computerized pick lists and automated calculation of physiological means and gradients and error checking. Data collection procedures were based on prior reliability studies [9]. Patient identifiers were removed from the database, and informed consent was waived by our institutional review board. Mean, standard deviation and P values were reported for comparisons. Wilcoxon and Chi-squared statistics were used to determine significance. Significance was considered at the P < 0.05 level.

Results

Eighty patients were identified with 21 (26%) in the LRM group, and 59 (74%) in the AT group. Compared to LRM

group, AT group had similar age in years (75 ± 13 vs. 72 ± 17, P = 0.4), similar gender (male: 56% vs. 52%, P = 0.8), similar pre-tPA National Institutes of Health stroke scale (NIHSS) (16 ± 9 vs. 14 ± 8, P = 0.4), and higher APACHE III scores (62 ± 26 vs. 41 ± 15, P = 0.0008) (Table 3). ICU length of stay in days was 2.5 ± 1.3 for the LRM group versus 4.5 ± 4.4 for the AT group (P = 0.04). ICU mortality was 4.7% (one patient DNR/hospice care) for the LRM group compared to 22% for the AT group (OR: 5.6; 95% CI: 0.7 - 46.0, P = 0.1). Hospital mortality was 4.7% for the LRM group compared to 36% for the AT group (OR: 11; 95% CI: 1.4 - 88.0, P = 0.02) (Table 3, Fig. 1).

Discussion

In this study, we present a model that identifies a group of acute ischemic stroke patients who received tPA who might be too well to benefit from neuroICU admission. This model is not intended to triage individual admissions because it uses treatment and physiological data obtained during the first ICU day. It can, however, be used to identify patient groups based on characteristics and outcomes retrospectively; that management can be

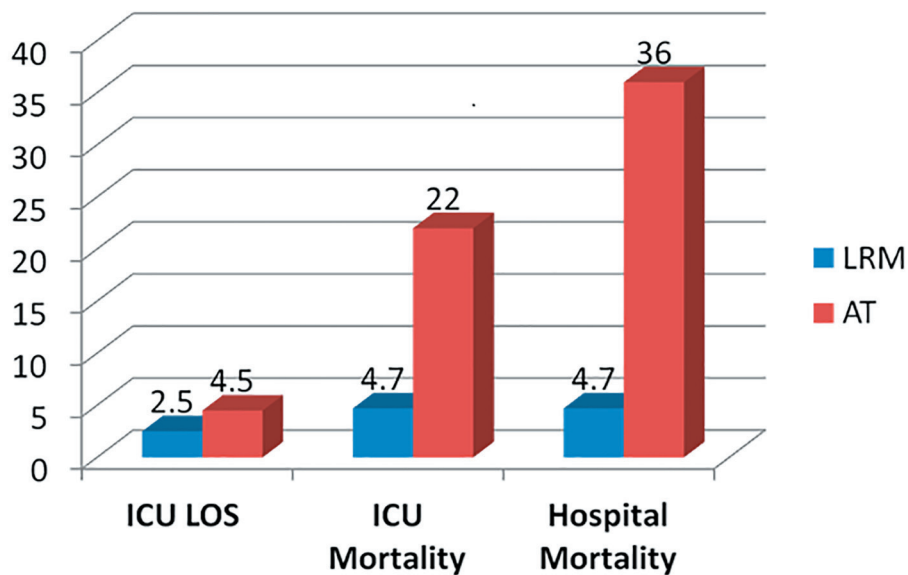


Figure 1. Outcome comparisons between the low risk monitor (LRM) and active treatment (AT) groups.

used to formulate policies, protocols, and educational programs pertaining to finding alternatives to admission to neuroICU.

The finding of this study confirms the result of the study by Zimmermann and Kramer, where this model was validated and successfully applied in the general ICU. To our knowledge, this is the first study of its kind to test this model on acute stroke patients who received tPA. The ability to identify LRM admissions can be used to support the development of intermediate care beds and step down units to care for LRM patients and to avoid the cost of constructing additional ICU beds, especially with scarcity of resources [10, 11].

Our study has several limitations. This is a single center study with a small number of patients, and this model may not apply to other neuroICUs; hence this would need to be studied in a large multicenter trial before it can be adopted for planning and management purposes. This model is thus not intended to triage individual admissions because it uses treatment and physiological data obtained during the first ICU day and not prior to ICU admission. For these reasons, ICU admission decisions for individuals still need to take into account physician judgment in addition to the characteristics of patient groups. In addition, the list in Table 1 does not include all possible treatments that might be required in a neuroICU, such as the need for assisted airway clearance which may be crucial in some stroke patients. ICU admission may be avoided, however, when services such as airway clearance, monitoring, and frequent neurochecks can be provided in non-ICU areas, such as intermediate care units.

Conclusion

The outcome of LRM patients in this study with ischemic stroke post-tPA suggests that they may not require admission to a formal neuroICU. Care of the LRM patients may be accomplished in an intermediate care unit, improving resource use and reducing costs. This model will need to be validated in other neuroICUs before it can be adopted.

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