Predictors of Need for Critical Care Support, Adverse Events, and Outcome after Stroke Thrombolysis

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Background: Results from trials and international registries exhibit heterogeneity regarding safety, efficacy, markers of prognosis, and markers of the need for critical care support after intravenous thrombolysis (IVT) for strokes. The purpose of our study was to indentify such markers after performance of comparisons among patients who received thrombolysis in our intensive care unit. *Materials and Methods:* Our study included 124 patients who received IVT in accordance with international criteria. Outcome measures of univariate and regression analyses resulted from comparisons between groups of patients with or without the need for critical care support (advanced life support and neurocritical care interventions), groups of patients developing or not developing primary adverse events (symptomatic intracranial hemorrhage [SICH] and/or Death and/or Serious systemic bleeding and/or New stroke) and groups of patients with different main outcome variables (mortality, functional independence at 3 months). *Results:* Our results suggested that higher severity scores (Simplified Acute Physiology Score II, National Institutes of Health Stroke Scale) correlated with the need for critical care support, primary adverse events, and main outcome variables, whereas older age was significantly associated with fewer adverse events. Hyperlipidemia, symptom-to-needle time, and vascular disease were associated with functional capacity at 3 months, whereas diabetes mellitus and vascular disease correlated with the need for critical care support. *Conclusion:* Patients' age, hyperlipidemia, presence of vascular disease, Simplified Acute Physiology Score II (a novel marker), and National Institutes of Health Stroke Scale at 2 hours and at 7 days are independent predictors of the need for critical care support, adverse events, and clinical outcomes after thrombolysis. **Key Words:** Ischemic stroke—SAPS II—thrombolysis—outcome—NIHSS.
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Introduction

Acute ischemic strokes remain one of the leading causes of morbidity, mortality, and disability worldwide,[1] despite major advances regarding their management. One of the most promising interventions for ischemic strokes is intravenous thrombolysis (IVT). When it is performed within the therapeutic window and in accordance with international guidelines,[2,3] it improves functional outcome and appears to be both safe and well tolerated.

Centers in Europe, the United States of America (USA), and other counties use different inclusion criteria,[2,3] different definitions for symptomatic intracranial hemorrhage (SICH)[4] and other thrombolysis complications, and different scales for evaluation of functional outcome.[5] This diversity leads to confusion regarding thrombolysis efficacy and outcome. When 1 center's experience is brought under investigation, it allows evaluation of everyday clinical practice in thrombolysis. We conducted this study in our center to contribute to this effort for better understanding of thrombolysis parameters and results.

Furthermore, the need for prognostic markers and markers of critical care need is obvious, and is strongly emphasized by international literature.[6] If we could predict which patients have greater risk for complications and worse clinical outcome, this would allow better decision making regarding who will receive thrombolysis and closer monitoring for those who are more likely not to achieve good results after thrombolysis and end up in an intensive care unit (ICU).

The aim of the current study was to investigate possible clinical or epidemiologic prognostic factors correlating with critical care need, complications, and clinical outcome.

Materials and Methods

In the absence of High Dependency Unit and Neurology Department in our hospital and Stroke Unit in our territory, IVT is performed at the ICU of General Hospital of Larissa. It is the only facility in our hospital in which IVT can be performed according to international standards[2,3] (vigorous noninvasive blood pressure monitoring and monitoring of the rest of the vital signs, frequent assessment of oxygen saturation and Glasgow Coma Scale, evaluation for the occurrence of complications, especially for the first 24 hours).

According to our hospital's protocol at the emergency department, triage is applied for identification of patients with symptoms of acute ischemic stroke. Those who are eligible for thrombolysis are vigorously brought to the ICU after having a brain computed tomography (CT) scan. Standard international protocols for thrombolysis[2] are used. Demographic characteristics, baseline clinical data, severity scores (Simplified Acute Physiology Score II [SAPS II]), and details regarding thrombolysis procedures

(symptom-to-needle time, actilyse dose, CT imaging details) are recorded. Patients' neurologic status is evaluated using the National Institutes of Health Stroke Scale (NIHSS) before thrombolysis and at 2, 24 hours, and 7 days after thrombolysis. All patients undergo the appropriate diagnostic workup for the cause of the stroke (transthoracic/transesophageal heart ultrasound, Holter monitor of heart's rhythm, triplex vascular ultrasound for evaluation of carotids and cerebrovascular circulation) and start secondary prevention (anticoagulation, statins). Those without complication, within 24 hours and right after a second brain CT scan that confirms the absence of intracranial hemorrhage, are discharged from the ICU and transferred either to the general medicine departments of our hospital or to the Neurology Department of Larissa University Hospital, if more specialized diagnostic tests are required (molecular thrombophilic tests, test for vasculitis, etc.). However, in case of complication (SICH, aspiration, reduction of level of consciousness, brain edema), patients remain in the ICU and receive the appropriate advanced life support or neurocritical care intervention (intubation, craniectomy, intracranial pressure monitoring, multimodal brain monitoring, etc.).

Patients were re-evaluated at 3 months after thrombolysis, regarding their medication use (anticoagulants, statins), and their performance/disability status, by means of the modified Rankin Scale (mRS). Every patient who has received IVT is enrolled at our local ICU thrombolysis database and at the international Safe Implementation of Treatments in Stroke—International Stroke Thrombolysis Register (SITS-ISTR).

Our 10-year (2004-2014) thrombolysis database was retrospectively evaluated and included a total of 124 patients with acute ischemic stroke, with a mean age of 65 years and a median NIHSS at admission 11 (range 2-28). They fulfilled international inclusion criteria.[2] However, 41 (33.1%) of them had 1 or more license contraindications to alteplase[7] or relative contraindications to thrombolysis.[2,3,8,9] In particular 10 patients were more than 80 years old, 13 patients had mild stroke with an NIHSS less than 5, and 22 patients had symptom-to-needle time of 3-4.5 hours. The relevant demographic and clinical data of our patients are shown in Table 1.

Database retrieved data included demographic characteristics, patients' medical history regarding predisposing factors (diabetes mellitus, arrhythmia, hypertension, smoking habit, hyperlipidemia, vascular disease, former ischemic stroke), severity scores (SAPS II at 24 hours, NIHSS at various time points), the therapeutic window (symptom-to-needle time), critical care need (patients who demanded advanced life support and neurocritical care interventions), all primary adverse events, mortality, and functional independence at 3 months.

All procedures performed in our study were in accordance with the ethical standards of the institutional or national research committee, and with the 1964 Helsinki