Safety and Efficacy of Mechanical Thrombectomy in Acute Ischemic Stroke of Anticoagulated Patients—A Prospective Observational Study

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Background: Anticoagulated patients (APs) are excluded from the acute stroke management with alteplase in Europe, not in the United States. They could benefit from mechanical thrombectomy (MT), which was not undoubtedly proven. There are scarce data about its results in such patients. The authors' aim is to analyze the efficacy and safety of MT in APs presenting with an acute stroke in our institution. *Methods:* Prospective observational study comparing 30 APs and 109 non-anticoagulated patients (N-APs) underwent direct MT without alteplase. Demographic data, clinical severity (National Institutes of Health Stroke Scale [NIHSS]), efficacy (recanalization thrombolysis in cerebral infarction [TICI] ≥ 2b and modified Rankin Scale score ≤ 2 at 3 months), and security (symptomatic intracranial hemorrhage [SICH], mortality at 3 months) were compared between both groups. *Results:* In both groups men were more frequent (63.3% of APs were men and 61.5% of N-APs were men). Mean age was 73 in APs and 67.2 in N-APs. Median NIHSS was similar (17 APs; 16 N-APs), also TICI greater than or equal to 2b (93.3% APs; 89.9% N-APs). The 3-month modified Rankin Scale score less than or equal to 2 was 46.7% in APs and 55.2% in N-APs ($P = .40$). SICH was present in 16.7% of APs and 8.3% of N-APs ($P = .15$). Mortality at 3 months was 6.7% in APs and 19% in N-APs ($P = .08$). *Conclusions:* MT is a valid treatment option in APs. It achieves an efficacy as in N-APs with a tendency to suffer more from SICH, but lower mortality. We hypothesize that cardioembolic clots may be easier to be removed than atherotrombotics, and that embolic stroke in APs might be less severe than that in N-APs or might suffer less of other complications than atherotrombotics.

Key Words: Anticoagulants—cerebrovascular disorders—revascularization—stroke—thrombolysis.

Introduction

Until very recently, intravenous alteplase (recombinant tissue plasminogen activator [rtPA]) administered within 4.5 hours after symptom onset has been the only reperfusion therapy with proven efficacy in patients with acute ischemic stroke.[1] However, this treatment has a lot of well-known absolute and other relative contraindications, such as anticoagulation therapy. Alteplase is approved in anticoagulated patients (APs) with International Normalized Ratio (INR) less than 1.7 in the United States, but not in Europe, where current use of anticoagulation is still a limitation for intravenous thrombolysis regardless of the INR.[2,3]

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Moreover, proximal arterial occlusions are more likely to fail treatment with intravenous rtPA, as it only achieves early recanalization in about one third of patients with terminal internal carotid occlusion,[4] the prognosis generally being poor in these cases.[5] Taking into account the numerous limitations of intravenous alteplase, different intra-arterial recanalization approaches have been developed during the last 20 years.[6-11] Some of them achieve higher rates of recanalization in proximal occlusions, but they have not been able to demonstrate better functional prognosis until now.[12-16] As a consequence, there are scarce data about the results of mechanical thrombectomy (MT) in certain subgroups of patients such as APs compared with non-anticoagulated patients (N-APs).

Our aim is to analyze the efficacy and safety of MT with stent retriever in APs, comparing the results with N-APs and nonreceivers of intravenous alteplase.

Methods

This is a prospective observational study comparing 30 APs with current use of dicumarins and 87 N-APs treated with direct MT with a stent retriever. All patients who had received any dose of alteplase were excluded. Patients with INR greater than 3.5 or activated thromboplastin time ratio (ATPTr) greater than 2 were also excluded. Upon arrival at the hospital, patients suffering acute stroke underwent the clinical practice established protocol, according to the ethical committee from our hospital. The time window for beginning the intervention is 4.5 hours for anterior circulation and 12 hours for basilar territory, and multimodal cranial tomography (CT) is practiced in every patient under consideration for MT, according to the previous mentioned protocol. Sometimes, when time of onset and multimodal CT were unclear, a magnetic resonance (MR) was carried out. In all cases, the infarct core according to the cerebral blood volume (CBV) was less than a third of the affected tissue, measured by mean transit time (MTT) and time to peak (TTP) in multimodal CT. A clinical–radiological mismatch was also demonstrated.

Demographic data and cardiovascular risk factors were compared between both groups. Clinical severity of stroke was compared at admission according to the National Institutes of Health Stroke Scale (NIHSS).[17]

Efficacy of MT was analyzed in terms of arterial recanalization according to the thrombolysis in cerebral infarction (TICI) scale,[18] assuming recanalization when TICI greater than or equal to 2b was achieved, and functional outcome by modified Rankin Scale (mRS), considering the prognosis to be good when mRS score is less than or equal to 2 at 90 days.[19]

Safety was evaluated according to symptomatic intracranial hemorrhage (SICH), defined as any intracranial, intraventricular, or subarachnoid hemorrhage associated with a 4-point or greater worsening on the NIHSS within the admission period, and mortality rates at 3 months. Other neurologic and systemic complications were also recorded. Causes of death and time of death were also described.

Statistical analysis was performed with the free distribution software R.2.10 (www.r-project.org). Quantitative variables were characterized by either the mean and standard deviation or the median, minimum and maximum values, depending on whether or not they were normally distributed. For categorical variables, absolute and relative frequencies were employed.

For comparison between groups, either parametric (Student's *t*-test, analysis of variance) or nonparametric tests (Mann–Whitney *U*-test, Kruskal–Wallis test) were employed on quantitative variables, depending on the Kolmogorov–Smirnov test for normality with Lilliefors correction. For categorical variables, the χ^2 test with exact significance was used. The cutoff point for statistical significance was $P < .05$ in all cases.

Results

Epidemiological and Demographic Characteristics

Between June 2012 and December 2014, a total of 117 patients fulfilled the inclusion criteria for this study. Eighty-seven of the patients were N-APs and the remaining 30 were APs. APs were older (N-APs 67.07 ± 10.60; APs 72.8 ± 7.85; $P = .007$) and had a more frequent history of hypertension (N-APs 55.9%; APs 80%; $P = .039$) and cardioembolic sources, such as atrial fibrillation and prosthetic valves (N-APs 11.11%; APs 87.49%; $P < .001$). There is also a nonsignificant tendency to use more antiplatelets in N-APs (N-APs 39.13%; APs 7.69%; $P = .095$). The rest of the epidemiological and demographic characteristics were similar between both groups as Table 1 details.

The reasons for avoiding alteplase in N-APs were as follows: recent major surgery (2.28%); stroke on awakening (7.6%); previous intracranial hemorrhage (ICH) (3.42%); recent stroke (4.56%); out-of-time window (36%); hypovolemic shock (1.14%); and large-vessel occlusion (45%).

Stroke Characteristics and Management

When analyzing the stroke etiology according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) scale,[20] cardioembolic stroke was significantly related to the AP group (N-APs 39.75%; APs 80%). However, the mean INR was 1.78 ± .71. In the N-AP group, atherothrombotic etiology was predominant (N-APs 26.50%; APs 3.33%). Details about etiologies are shown in Table 2. Patients' locations after the procedure (stroke unit versus intensive care unit) were similar in both groups, as approximately two thirds of the patients were admitted to the stroke unit in both groups. There were no differences in the type of anesthesia, either being mainly sedation