Curitiba acute ischemic stroke protocol
A university hospital and EMS initiative in a large Brazilian city

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ABSTRACT
Few healthcare centers in Brazil perform thrombolytic therapy for acute ischemic stroke (AIS) patients. **Objective:** The aim of this study was to describe an interinstitutional protocol for the rapid identification and thrombolytic treatment of AIS patients at a public health hospital in a large Brazilian city. **Method:** Emergency medical services (EMS) personnel evaluated 433 patients with possible stroke during a six-month period. After a standard checklist, patients with suspected AIS and symptoms onset of less than two hours were evaluated at our University Hospital (UH). **Results:** Sixty-five (15%) patients met the checklist criteria and had a symptom onset of less than two hours, but only 50 (11%) patients were evaluated at the UH. Among them, 35 (70%) patients had ischemic stroke, 10 (20%) had hemorrhagic stroke, and 5 (10%) had other diagnoses. Of the 35 ischemic stroke patients, 15 (43%) underwent IV thrombolysis. **Conclusion:** The present study demonstrated that trained EMS workers could help to improve the rate of thrombolytic treatment in large Brazilian cities. Permanent training programs for EMS and hospital staff, with quality control and correct identification of AIS patients, should be implemented to increase appropriate thrombolytic therapy rates in Brazil.

Key words: acute ischemic stroke, thrombolytic therapy, emergency medical services, stroke therapy, hospital management.

Protocolo de AVCi agudo em Curitiba: uma iniciativa de um hospital universitário e do SAMU

RESUMO
No Brasil, apenas alguns hospitais realizam terapia trombolítica para o acidente vascular cerebral isquêmico agudo (AVCiA). **Objetivo:** O objetivo deste estudo foi descrever um protocolo inter-institucional para a rápida identificação e para o tratamento trombolítico de pacientes com AVCiA em hospital público de Curitiba, PR. **Método:** O Serviço de Atendimento Médico de Urgência (SAMU) avaliou 433 pacientes com possível AVC durante um período de seis meses. Depois de um check list padrão, os pacientes com suspeita de AVCiA e início dos sintomas inferior a duas horas, foram avaliados no Hospital de Clínicas (HC). **Resultados:** Sessenta e cinco (15%) pacientes preencheram os critérios propostos, porém apenas 50 pacientes (11%) foram avaliados no HC. Destes, 35 (70%) eram AVCiA, 10 (20%) eram hemorrágicos e 5 (10%) tiveram outros diagnósticos. Dos 35 pacientes com AVCiA, 15 (43%) foram submetidos a trombólise IV. **Conclusão:** O presente estudo demonstrou que o treinamento do SAMU poderia auxiliar na otimização da terapia trombolítica em grandes cidades brasileiras. Programas permanentes de treinamento com controle de qualidade, caracterizados pela correta identificação de pacientes com AVCiA devem ser realizados nos hospitais em parceria com o SAMU para elevar as taxas de tratamento trombolítico no Brasil.

Palavras-chave: acidente vascular cerebral isquêmico agudo, terapia trombolítica, serviços médicos de urgência, condutas hospitalares.
Stroke is a leading cause of disability and mortality in Brazil. Despite the reduction in associated mortality over the last 30 years, the incidence of stroke remains high (between 61.8 and 105.4 per 100,000 inhabitants), as does the mortality rate (between 23.9 and 40.9 per 100,000 inhabitants)\(^7,8\). This has two major causes: [1] the majority of the Brazilian population is not well informed about stroke or its symptoms, and [2] prevention management is not consistent between the different regions of the country\(^1,3,4\). Although the “Serviço de Atendimento Móvel de Urgência” (SAMU), an emergency medical service (EMS), was initiated in some Brazilian cities in 2003, no standard protocol has been developed that would allow EMS providers to correctly identify acute ischemic stroke (AIS) patients. Previous studies have demonstrated that a number of measures, such as public education programs, professional educational programs within health systems, and the creation of stroke teams and hospital and ambulance protocols, can all increase the use of thrombolysis in AIS\(^5,6\). The aim of this study was to describe the importance of cooperation between the SAMU and a local university hospital (UH) in the introduction of thrombolytic therapy in Curitiba, Brazil.

**METHOD**

The study subjects were all patients with suspected AIS and a symptom onset of less than two hours prior who were seen by the SAMU in Curitiba, a Brazilian city with 1,797,408 inhabitants, from July 2007 to December 2007. The patients were evaluated using a standard checklist based on the Los Angeles Prehospital Stroke Screen (LAPSS) and thrombolytic criteria, which were partially based on the National Institute of Neurological Disorders and Stroke (NINDS) study\(^7,8\). After completing this checklist, SAMU personnel contacted the in-hospital neurologist at Hospital de Clínicas from Universidade Federal do Paraná and took the patient directly to the hospital’s computed tomography (CT) scan room, where the neurologist, laboratory staff, and CT scan technicians were waiting. A brain CT scan was obtained following a concise clinical and neurological examination by a neurologist certified in NIHSS examination, and eligibility for thrombolytic treatment was individually determined based on the inclusion and exclusion criteria described in the NINDS study\(^8\). Patients who underwent thrombolysis were admitted to an emergency room for continuous monitoring and a complementary diagnosis, which included transcranial Doppler and electrocardiography, IV recombinant tissue plasminogen activator (rtPA) administration based on the NINDS protocol, and intensive monitoring for the next 24 hours. This study was authorized by the hospital ethics committee.

Patients who were deemed ineligible for IV rtPA were sent to a primary medical center for general treatment and secondary prevention. All of the included patients were followed in the outpatient cerebrovascular disease clinic of the UH.

We analyzed the mean time from stroke symptom onset to first contact with the neurologist via the SAMU (sympt-neuro time), the mean time from symptom onset to the patient’s arrival at the hospital (sympt-door time), the mean time from SAMU contact to the patient’s arrival at the hospital (cont-door time), and the clinical diagnosis after neurological evaluation for patients who were diagnosed with an ischemic stroke.

For the ischemic stroke group, the clinical symptoms and the CT findings were categorized according to previously published criteria\(^9,10\). The time of symptom onset and the time of day were evaluated and compared between the thrombolysed (rtPA) and non-thrombolysed (non-rtPA) groups. Onsets between 6 AM and 6 PM were considered daytime onsets, and onsets between 6 PM and 6 AM were considered nighttime onsets. Outcome variables were the median NIHSS score 24 hours after treatment and the modified Rankin score (mRS) after three months. These variables were compared between the rtPA and non-rtPA groups. We also analyzed the exclusion criteria according to the NINDS protocol for patients in the non-rtPA group. The mean time from patient’s arrival at the hospital and medication infusion (the door-to-needle time) was analyzed in the rtPA group.

A hemorrhagic transformation was defined as a hemorrhagic infarction (HI) in which a petechial infarction without a space-occupying effect was demonstrated, and a parenchymal hemorrhage (PH) was defined as a hemorrhage with a space-occupying effect\(^11,12\). HIs were further categorized as HI1 (small petechiae) or HI2 (more confluent petechiae); PHs were further categorized as PH1 when the hematoma involved less than 30% of the infarcted area and as PH2 when the hematoma involved at least 30% of the infarcted area or a clot was detected at some distance from the infarcted area\(^11\). A symptomatic hemorrhagic transformation (HT) was defined as brain imaging evidence of HT with clinical worsening, indicated by an NIHSS score increase of at least four points\(^12\).

Statistical analyses were performed with SPSS 12.0 software (SPSS, Inc). Statistical significance was assessed by Student’s t-test or the Mann-Whitney test for continuous variables and the chi-squared test for categorical variables. Statistical significance was set at p<0.05.

**RESULTS**

During the study period, the SAMU evaluated 433 patients with stroke symptoms. Sixty-five (15%) had a symptom onset shorter than two hours prior, and only
50 (76%) of these were transferred to the UH after being identified as potentially eligible for IV thrombolysis. The other 15 (24%) were not identified by the EMS as AIS, and they were not included in the current prospective protocol. Among the 50 patients evaluated, the mean age was 64.36±15.84 years (range: 23 to 86 years), and 27 were female. Based on neurological evaluations and brain CTs, 45 (90%) patients were diagnosed with stroke, three (6%) were diagnosed with TIA, one (2%) was experiencing a postictal state after a convulsive seizure, and one (2%) was diagnosed with a psychogenic event (Fig 1).

Of the 45 stroke patients, 10 (22%) had hemorrhagic strokes. Thrombolysis exclusion criteria were identified in 43% of the patients: seven (15%) arrived more than three hours after symptom onset but were correctly identified as having an AIS by the EMS personnel; one (2%) had uncontrolled arterial hypertension, one (2%) had a platelet level less than 100,000/µl, and eleven (24%) displayed good spontaneous clinical improvement within minutes after hospital arrival (a median NIHSS reduction from 3 to 1 after the first evaluation). Excluding the hemorrhagic stroke patients, the non-rtPA group included the other 20 AIS patients for whom thrombolytic therapy was contraindicated. The remaining 15 patients were treated with rtPA and included in the rtPA group, which represented 3.4% of all the patients evaluated by the EMS. The NIHSS scores of the 35 AIS patients were between 1 and 21, and 12 (34%) patients had NIHSS scores ≤4. The symp-neuro times, symp-door times, and cont-door times are shown in Table.

Only three (20%) patients in the rtPA group had symptoms that began at night, compared with ten (50%) from the non-rtPA group (p=0.07). Cortical symptoms were more common in the rtPA group (73%) than the non-rtPA group (40%) (p=0.05). Of the patients diagnosed with a middle cerebral artery ischemic stroke (14 in the rtPA group and 8 in the non-rtPA group), an ASPECTS value >7 was found in 10 subjects in the rtPA group and 7 in the non-rtPA group (p=0.127). The door-to-needle time for the rtPA group is presented in Table 1. In this group, 13 patients were treated within 60 minutes of arrival, and all were treated within 90 minutes of symptom onset.

The median pre-treatment NIHSS score was worse in the rtPA group (NIHSS=16) than in the non-rtPA group (NIHSS=4; p=0.004). Nevertheless, both groups presented a good recovery after 24 hours (NIHSS=9 in the rtPA group and 3 in the non-rtPA group; p=0.160), as shown in Fig 2. Notably, 40% of the patients in the rtPA group had an NIHSS score higher than 16 at hospital admission.

After three months of follow-up, we observed similar median mRS values in the two groups (mRS=2 in both the rtPA and non-rtPA groups; p=0.520; Fig 2). An mRS score ≤2 points was observed in 8 (53%) patients from the rtPA group and 12 (60%) from the non-rtPA group (p=0.744), and an mRS score ≤1 was seen in 33% and 40%, respectively (p=0.735). In the rtPA group, three patients (20%) developed intracranial hemorrhages; one had a PH2, and the other two had an HI2. No patients

Table. Time variables for 35 ischemic stroke patients admitted to the university hospital.

<table>
<thead>
<tr>
<th>Time variables</th>
<th>rtPA group (n=15) Median±SD</th>
<th>Non-rtPA group (n=20) Median±SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symp-neuro time (minutes)</td>
<td>64.26±39.01</td>
<td>146.30±183.64</td>
<td>0.066</td>
</tr>
<tr>
<td>Symp-door time (minutes)</td>
<td>86.06±42.13</td>
<td>203.20±180.70</td>
<td>0.009</td>
</tr>
<tr>
<td>Contact-door time (minutes)</td>
<td>18.80±9.68</td>
<td>56.90±28.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Door-to-needle time (minutes)</td>
<td>54.13±21.36</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*Symp-neuro time: the mean time from symptom onset to a neurologist being contacted by the SAMU-Curitiba; **Symp-door time: the mean time from symptom onset until the patient arrived at the hospital; **Contact-door time: the mean time from SAMU contact until the patient arrived at the hospital. All times are in minutes.

Fig 1. Flowchart for patients admitted to the university hospital.
**DISCUSSION**

This study is the result of the combined efforts of municipal health agencies and a local UH to introduce thrombolytic therapy to the Brazilian public health system. We demonstrated that a protocol for the treatment of AIS patients can work properly with cooperation between a UH and a prehospital EMS, with correct acute stroke identification in the majority of the patients who were evaluated by the EMS team. Implementing this type of cooperative treatment approach is important because 50% to 60% of all stroke patients are AIS patients who were evaluated by the in-hospital neurologist; thus, adequate cooperation between the EMS and the hospital directly impacts both the time before proper treatment is initiated and the stroke outcome.\(^5,13\)

If a suspected stroke is not regarded as an emergency, AIS patients can easily miss the time window necessary for thrombolytic treatment, reducing the likelihood of stroke recovery.\(^5,6,14-16\) Fifteen (14%) patients were not identified by EMS personnel as AIS, and they were not included in the current prospective protocol. In addition, the percentage of patients who met the exclusion criteria for thrombolysis in this study was similar to that in previous studies.\(^7,18\)

In the current study, we observed that patients with untreated AIS had longer symp-door times and cont-
crease primary prevention and rapid diagnosis as well as reduce time to treatment; and [d] the inclusion of tertiary hospitals in different city regions to increase the number of patients with AIS who are adequately diagnosed and treated. According to our experience, cooperation between EMS teams and a local UH permits the use of efficacious thrombolytic therapy in a public system setting. EMS triage personnel who are adequately trained to identify eligible patients for IV thrombolysis are critical to the success of such an ambitious venture. Although the treated patients presented with worse NIHSS measures at stroke onset, their recovery outcomes were similar to those of non-thrombolysed patients.

Efforts should be made to increase appropriate thrombolytic therapy rates in our country. A Brazilian initiative for adequate and prompt acute stroke management should be instituted not only for neurological services but also for prehospital teams and all emergency medical services.

REFERENCES