

# ARE WE READY FOR INTRAVENOUS THROMBOLYSIS IN ACUTE STROKE TREATMENT IN OUR REGION?

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**SUMMARY** – Acute stroke is the leading cause of disability in modern society. Early treatment is crucial to maximize the benefit of stroke intervention. Effective thrombolytic therapy is dependent on timely intervention and guidelines for the recommended use of recombinant tissue plasminogen activator therapy within 3 hours after onset of stroke symptoms. The aim of the study was to assess whether we are ready for the introduction of thrombolysis in our region. We investigated retrospectively the time from symptom onset to hospital arrival (delay time) for patients with acute stroke in our region. Medical histories of all patients admitted to the Department in 2006 with acute stroke symptoms were studied. Statistical analysis was performed by use of the SigmaStat (version 2.0) software. Study results showed that a very high rate of patients presented after 24 hours of stroke onset (35%); 15% of all acute ischemic stroke (AIS) patients arrived within 3 hours of stroke onset. Due to other exclusion criteria established, only 4% of all AIS patients were eligible for intravenous thrombolysis. Most patients arrived in the hospital too late to get maximum benefit from the emerging stroke therapies. This may be due to the failure to recognize signs and symptoms or the lack of awareness of the potential treatment benefits. Our further efforts should be focused on increasing public awareness of the stroke signs and symptoms and on reducing delay time.

**Key words:** *Stroke; Thrombolytic therapy; Time factors; Hospitalization*

## Introduction

Acute stroke is a major cause of disability and death in Croatia<sup>1-3</sup>. The increased incidence of stroke<sup>4,5</sup> in Croatia has been presumed to be the consequence of poor public stroke awareness, low and inadequate risk factor identification and control, and inadequate action planned. In a previous study, public awareness of the stroke signs and risk factors in our region was found to be inadequate<sup>6</sup>. It is well known that intravenous thrombolysis (IVT) with recombinant tissue plasminogen activator (rt-PA) is the only specific treatment approved for cerebral infarction<sup>7</sup>. However,

effective thrombolytic therapy is dependent on timely intervention and guidelines for the use of rt-PA within 3 hours after the onset of stroke symptoms<sup>8,9</sup>.

Therefore, we investigated the time from symptom onset to hospital arrival (delay time) for patients with acute stroke in our region and the percent of patients which could get maximum benefit from the emerging stroke therapies.

## Methods

Medical histories of all patients admitted to the Department in 2006 with acute stroke symptoms were investigated. We studied all medical records, demographic data, risk factors and time aspects, and compared them with the well-known guidelines. All patients had their stroke severity assessed with the National Institutes of Health Stroke Scale (NIHSS),

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with scores ranging between 0 and 38 at admission categorized as mild (0-6), moderate (7-15), or severe (16-38). Statistical analysis was performed by the SigmaStat (version 2.0) software. Descriptive statistics was used for demographic data.

## Results

Out of 1118 hospitalized patients in 2006, 388 had symptoms indicative of acute ischemic stroke. Out of 388 patients, 327 (84%) had ischemic stroke, 41 (10.5%) hemorrhagic stroke, 15 (4%) subarachnoid hemorrhage and 5 (1.5%) subarachnoid and cerebral hemorrhage. Their mean age was  $72.5 \pm 10.1$ , with slight predominance of female patients (50.8%) and urban population (51%). Considering risk factors, 97.9% had hypertension, 42.2% atrial fibrillation and cardiomyopathy, 29.6% diabetes mellitus, 27.3% hyperlipidemia, 2% alcohol and 1.8% smoking. Median NIHSS score at admission was  $10.2 \pm 2.2$ ; 28.6% of all stroke patients were transferred to rehabilitation centers, and 21% of all admitted patients died. The mean value of Barthel index at discharge was  $87.5 \pm 12.1$ . The exact time of stroke onset was known in 94.5% of study patients. The median time from symptom onset to hospital emergency room arrival was 600 minutes. We found a very high rate of patients presented after 24 hours of stroke onset, even 35%. All of them were from rural areas of the region. Fifty (15%) of 327 patients with acute ischemic stroke arrived within 3 hours of stroke onset, all of them by the Emergency Medical Service (EMS). Most (70%) of these early presented patients had symptoms of a severe stroke (NIHSS >16); 38% (n=125) of all patients with acute ischemic stroke arrived within 6 hours and 22% (n=75) of them within 4.5 hours of stroke onset. Due to other exclusion criteria established, only 14 (4%) of all ischemic stroke patients were eligible for intravenous thrombolysis and maximum benefit from this treatment.

## Discussion

Our region is the longest and narrowest county in Croatia. There are some areas in our region that are more than 90 km far from our hospital, with very bad, narrow, winding, country roads. The study hospital has a catchment area of 176 765 inhabitants<sup>2</sup>. This

study was performed prior to introducing intravenous thrombolysis in our region.

The results of our study suggest that prehospital delay in patients with acute stroke was considerable in this area. There were long intervals between the onset of symptoms and hospital emergency room arrival (mean, 600 minutes), which is more than in some other studies<sup>10-13</sup>. This may be due to the failure to recognize the signs and symptoms or the lack of awareness of potential treatment benefits. A previous study pointed to inadequate public awareness of the stroke signs and risk factors in our region<sup>6</sup>. The results of that study have shown that the awareness of the stroke risk factors and warning signs should be increased through more effective community-based educational strategies, primarily mass media, to entail powerful response<sup>6</sup>. We have to focus on the population as a whole and on the groups at a high risk. It is possible that some patients did not come due to an inadequate response to the stroke signs, as seen in the previous study<sup>6</sup>. In some studies in Taiwan, patients reported that they did not realize the urgency of seeking for medical help<sup>14</sup>. Barber *et al.* noted that the patients who recognized their symptoms might choose not to seek medical attention<sup>15</sup>. A rather high percentage of 35% of all stroke patients who came after 24 hours of the stroke symptoms onset is discouraging. Some studies in Buffalo Metropolitan area and Erie County also showed 26% of all stroke patients to have come after 24 hours of the onset of stroke symptoms. Another study found time intervals between symptom onset and hospital arrival to be 0 to 3 hours in 21%, 3 to 6 hours in 11%, 6 to 24 hours in 19% and undetermined in 22% of patients<sup>16</sup>.

Only 15% of patients reached the hospital emergency room within 3 hours of symptom onset. Due to other exclusion criteria established, 4% of all ischemic stroke patients were eligible for intravenous thrombolysis and maximum benefit from this treatment. This result is lower than those reported from other studies<sup>10-18</sup> and far from optimal in patients with acute stroke. All of them came by the EMS, which is a well-known way to shorten prehospital delay<sup>10-18</sup>. Since the EMS utilization by stroke patients is potentially modifiable and could be the best and the most direct way to increase the number of IVT treated stroke patients, improvement of the EMS infrastructure in our region

is needed, especially in those distant rural areas. Interventional programs, emphasizing stroke recognition and immediate and appropriate response (calling 94), should be developed. The reason for such a small percentage of patients eligible for intravenous thrombolysis may be the rather old population observed in our study, due to recent findings that an advanced age was significantly associated with the increased delay time, since they are less likely to know the symptoms of stroke<sup>14</sup>.

In our study, we observed that the patients experiencing severe stroke appeared to present early after symptom onset, as in some previous studies<sup>16-18</sup>. Evidently, more severe neurologic deficits in an acute stroke are perceived more often as life threatening and prompt patients to seek immediate help.

In conclusion, most patients arrive at our hospital too late to benefit maximally from the emerging stroke therapies. This may be due to the failure to recognize the signs and symptoms or the lack of awareness of potential treatment benefits. Our further efforts should be focused on increasing public awareness of the stroke signs and symptoms, disseminating guidelines and recommendations for stroke evaluation and treatment, and preparing population as a whole for introducing IVT for acute stroke in our region. If we develop initiatives including those targeting healthcare, emergency medical system and public at large, and more specifically target persons at risk of longer delay, we could reduce delays in hospital arrival after acute stroke and maximize the effectiveness of IVT.

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## Sažetak

## JESMO LI SPREMNI ZA INTRAVENSKU TROMBOLIZU U LIJEČENJU AKUTNOG MOŽDANOG UDARA U NAŠOJ REGIJI?

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Akutni moždani udar je vodeći uzrok invalidnosti u današnjem društvu. Rano liječenje je bitno za što veću učinkovitost akutnog liječenja. Učinkovita tromboliza rekombiniranim aktivatorom tkivnog plazminogena ovisi o vremenu i preporukama da se provede unutar 3 sata od nastanka simptoma moždanog udara. Cilj ove studije bio je utvrditi jesmo li spremni za uvođenje trombolize u našu regiju. Retrospektivno se promatralo vrijeme od nastanka simptoma do dolaska u bolnicu (vrijeme kašnjenja) bolesnika s akutnim moždanim udarom. Promatralo se se povijesti bolesti svih bolesnika primljenih u bolnicu u 2006. godini. U statističkoj obradi primijenjen je program SigmaStat (verzija 2.0). Utvrđen je vrlo visok postotak (35%) bolesnika koji su došli nakon 24 sata od nastanka moždanog udara; 15% svih bolesnika primljenih s akutnim ishemijskim moždanim udarom (AIMU) došlo je unutar 3 sata. Uzimajući u obzir i ostale kriterije isključivanja samo je 4% svih bolesnika primljenih s AIMU moglo primiti sistemsku trombolizu. Većina bolesnika je stigla prekasno da bi imala maksimalnu korist od hitne terapije moždanog udara. Uzrok je možda nepoznavanje znakova i simptoma ili nedovoljna saznanja o korisnosti ovog liječenja. Potrebno je i dalje se truditi i poboljšavati poznavanje znakova i simptoma moždanog udara, kao i smanjiti vrijeme kašnjenja.

Ključne riječi: *Moždani udar; Trombolitička terapija; Vremenski čimbenici; Hospitalizacija*