

TIME TO HOSPITAL ADMISSION IN PATIENTS WITH ACUTE STROKE – OBSERVATIONAL STUDY IN SPLIT – DALMATIA COUNTY, CROATIA

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SUMMARY – The objective of this prospective observational study was to determine and document the time elapsed from symptom onset to hospital admission in patients with acute stroke. The study was conducted at Emergency Department, University Department of Neurology, Split University Hospital in Split, Croatia, from October 1, 2004 to December 21, 2004, and included 115 patients with acute stroke. Data on the time of onset of stroke symptoms, brain computed tomography finding and current clinical status were noted. Fifteen patients were excluded from the study because the exact time of symptom onset could not be determined. A standardized interview with patients and/or their relatives was taken to collect the information needed. Ischemic stroke was diagnosed in 82 of 100 patients. Only 13 patients arrived in hospital within 3 hours of stroke symptom onset, and 29 were admitted to hospital more than 24 hours of stroke symptom onset. Sex had no significant effect on arrival time. It was concluded that the majority of patients with acute stroke did not present to emergency department within 3 hours of symptom onset, the current time window for thrombolytic therapy. It seems crucial to identify the factors associated with late presentation to the hospital. Public recognition of stroke symptoms and understanding of the importance of early hospital admission are mandatory for improving the results recorded in this study with time elapsed from symptom onset to hospital admission and eligibility for thrombolytic therapy taken as the main outcome measures. Additional public education is needed to increase awareness of the stroke warning signs.

Key words: *Cerebrovascular disorders – therapy; Cerebrovascular disorders – diagnosis; Acute disease; Hospitalization; Emergency medical services – statistics and numerical data; Disability evaluation*

Introduction

Stroke is one of the leading factors of long-term and permanent disability. The economic burden of stroke on society in the USA has been estimated to more than 50 billion USD *per* year¹. In addition, stroke is on the third place of all death causes in the world and the leading cause of death in Croatia². The provision of stroke care imposes a major economic burden of the national healthcare system.

Cerebrovascular diseases are the third most common cause of hospitalization among all cardiovascular diseases in Croatia. In 2002, the most common cause of hospitalization from the group of cerebrovascular diseases was cerebral infarction with 41%, followed by stroke unspecified as hemorrhage or infarction with 29.4%, and intracerebral hemorrhage with 8.3%².

Although some advances have been made in the treatment of acute stroke, the effectiveness of the new therapies is highly time-dependent³. Animal studies of cerebral ischemia suggest that the time window for effective therapeutic intervention may be only 4 hours⁴. Research in humans supports these data: the first proven treatment for acute stroke is efficacious when given within 3 hours of stroke onset⁵. Clinical studies suggest that cerebral ischemia persisting for more than 6 hours

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Received March 27, 2006, accepted in revised form October 9, 2006

results in permanent neurological damage⁶. Thus, early hospital arrival is critical to successful stroke treatment. Evidence from clinical trials⁵ suggests that ischemic stroke can be managed as a medical emergency and outcomes can be improved by using the thrombolytic agent recombinant tissue plasminogen activator (rtPA).

Early treatment is crucial in maximizing the benefit of stroke intervention and the time elapsed from stroke onset to hospital admission is critical in acute stroke management. Patients with stroke often arrive at the hospital too late to receive maximum benefit from new treatment modalities such as thrombolytic therapy. Rapid emergency care and admission to a specialized stroke unit is currently recommended for all patients with acute stroke⁷⁻⁹.

The most common reason for exclusion from thrombolytic protocol or other urgent therapeutic protocols and consecutively, the major factor limiting the use of new stroke therapies, is delay in presentation of stroke patients¹⁰⁻¹⁴. Delays in the treatment of stroke constitute a factor that leads to a more unfavorable prognosis¹⁵.

This is the second study taken in Split County in Croatia, which sought to determine the time to hospital admission in patients with stroke. Little is known about the presentation and early management of patients with acute stroke in Croatia. In this study, we collected some valuable information on delayed stroke unit admission of stroke patients at Split University Hospital in Split, Croatia.

Patients and Methods

This prospective study was performed from October 1, 2004 to December 21, 2004, at Emergency Neurology Department (END), University Department of Neurology, Split University Hospital, Split, Croatia. Split University Hospital has a large urban and rural catchment population of approximately 500,000 people. We prospectively studied 115 consecutive acute stroke patients presenting to our Department. We included all patients presenting with symptoms of the possible acute stroke. The aim of this population based study was to analyze the time to hospital arrival in stroke patients. When the stroke symptom onset could not be determined, patients were excluded from the study (n=15). Data were collected by physicians from patients, patient family members and medical records.

Stroke symptom onset was defined as the time when neurological deficit was first noticed by the patient or

an observer. If symptoms were first noticed on awakening, the stroke onset time was considered to be the time of awakening, because it represents the time when medical help could be sought. The length of delay from onset to admission was calculated on the basis of exact hour of onset and time of arrival in END. In all cases, the time of admission was defined as the time the patient presented to END.

Stroke was defined according to the World Health Organization definition as "rapidly developing clinical sign of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than of vascular origin"¹⁶. Patients with transient ischemic attack were excluded from analysis. The diagnosis of stroke was verified by a neurologist, and brain computed tomography (CT) scan was obtained in all cases.

Statistical analysis was done by use of Statistica® for Windows Program. The χ^2 -test was used to compare categorical variables considering time to hospital admission.

Results

During the study period, a total of 115 patients with symptoms of acute stroke were admitted to Department of Neurology, Split University Hospital in Split. Intracerebral hemorrhage was diagnosed in 18 and ischemic stroke in 82 patients, whereas 15 patients were excluded for incomplete data on the stroke symptom onset. Mean age was 68.9 (SD 15.2). Sixty percent of the study population were men. The exact time of stroke onset was determined in all patients. Fifteen patients died a few days after hospital admission. Thirteen patients (7 male and 6 female) arrived in hospital within 3 hours, 22 (13 male and 9 female) within 3-6 hours, 26 (16 male and 10 female) within 6-12 hours, 10 (6 male and 4 female) within 12-24 hours, and 29 (17 male and 12 female) more than 24 hours of stroke symptom onset.

Patients with hemorrhagic stroke were admitted after a statistically significantly ($p=0.0069$) shorter delay than those with brain infarction. The median delay in hemorrhagic stroke was 6 hours, and in brain infarction 12 hours.

Discussion

Early neurological attention is associated with better functional outcome and shorter hospital stay¹⁷. Several studies have demonstrated that delays in stroke

management have a significant effect on outcome¹⁸⁻²⁶. In these studies, the median time from onset to admission ranged from 4 hours to more than 24 hours. Some studies evaluated the factors associated with late arrival of acute stroke patients to hospital¹⁸⁻²⁶.

Delay in arrival of acute stroke cases may be caused by organizational, educational, geographical and demographic factors²⁷. Some of the reasons for delay may be attributable to different routes of access to hospital care. For this reason, the results of studies in one country or region may not be applicable elsewhere²⁸.

After years of therapeutic nihilism, there is now some optimism that effective treatments of stroke might become more widely available. Since September 2004, rt-PA has been approved in Croatia for acute stroke treatment. The effectiveness of rt-PA diminishes with time: the longer the delay, the smaller the probability of improving blood flow to the affected area of the brain and the greater the risk of hemorrhagic complications²⁸. Shortening the delay time in the health care of patients with suspected stroke is essential in order to reduce the morbidity and mortality rates of this disease¹⁵.

It is well known that prior to the occurrence of irreversible neuronal damage, an infarct passes through a "window period" of 3-6 hours during which it is salvageable if circulation is restored²⁹.

A similar study was already conducted in Split County in 2002 and showed better results than those found in the present study³⁰. The median time from stroke onset to admission to stroke unit in the study by Lušić *et al.* was 6.7 hours, and 24% of patients presented within 3 hours of stroke onset³⁰. Results of the present study showed the delay in presentation to be typical for most stroke patients. The majority of our stroke patients did not come to the hospital early enough to receive acute treatment with rtPA. Measures to reduce delay in arrival of acute stroke patients must be taken so that more patients could become eligible for new stroke therapy modalities.

Consistent with prior studies¹²⁻²⁶, we found that sex did not significantly influence arrival time. More fulminant onset of hemorrhagic stroke seems a logical explanation why such patients were admitted after a shorter delay than those with brain infarction²¹.

Some questions arising from this study need to be mentioned: it would be wise to identify and explore factors associated with delayed presentation of acute stroke patients in order to find measures to deal with them. Recent studies¹²⁻²⁶ have already shown that factors in-

fluencing arrival time of stroke patients are sex, age, stroke severity, mode of onset, stroke awareness, recognition of symptoms, mode of transport, level of patient education, marital status, familiarity with stroke symptoms and knowledge about stroke, and a few others.

A recent study by Rasmussen *et al.* showed that patients with stroke or transient ischemic attack in a Danish metropolitan area arrived at hospital at a median of 2.6 hours after the onset of stroke symptoms³¹. Maze *et al.* found that 28.9% of stroke patients arrived at the hospital within 3 hours of the first warning sign³². In different countries, time from the first signs of stroke to hospital admission varies greatly¹²⁻²⁶. One should ask: why people living in Split County cannot be admitted to hospital in time which gives them hope to survive and to receive the best treatment modalities currently available? A major challenge for people in Split County would be to increase the rate of admission within 3 hours of stroke onset to 50%. To achieve this goal, an analysis of the factors delaying admission is mandatory. Presentation of recent advances in acute stroke therapy amongst primary care physicians and public is essential to dispel the nihilistic attitude towards patients with stroke. Further efforts to increase public awareness of stroke signs and symptoms, to disseminate guidelines and recommendations for stroke evaluation and treatment, and to develop initiatives may reduce the time from stroke onset to treatment.

Public recognition of stroke symptoms and understanding of the importance of early hospital admission are mandatory for improving the results found in this study³³. We must put great effort in presenting stroke to the public and healthcare professionals as a medical emergency that should be treated at specialized stroke units as soon as possible after the onset of stroke symptoms. Our task is to promote public awareness of the benefits of prompt stroke treatment and the goal is reducing the time from stroke onset to efficacious treatment.

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Sažetak

VRIJEME DO PRIJEMA U BOLNICU KOD BOLESNIKA S AKUTNIM MOŽDANIM UDAROM
– OPSERVACIJSKA STUDIJA U SPLITSKO-DALMATINSKOJ ŽUPANIJI, HRVATSKA*I. Bilić, P. Filipović-Grčić i I. Lušić*

Cilj ove prospektivne opservacijske studije bio je utvrditi i dokumentirati vrijeme proteklo od nastupa simptoma do prijema u bolnicu kod bolesnika s akutnim moždanim udarom. Studija je provedena na Hitnom odjelu Klinike za neurologiju, Kliničke bolnice Split u Splitu od 1. listopada 2004. do 21. prosinca 2004. godine i uključila je 115 bolesnika s akutnim moždanim udarom. Bilježili su se podaci o vremenu nastupa simptoma moždanog udara, nalazu kompjutorizirane tomografije mozga i aktualnom kliničkom statusu. Iz studije je isključeno 15 bolesnika u kojih se točno vrijeme nastupa simptoma nije moglo utvrditi. Proveden je standardizirani razgovor s bolesnicima i/ili njihovom rodbinom kako bi se dobile potrebne informacije. Ishemijski moždani udar je utvrđen u 82 od 100 bolesnika. Samo je 13 bolesnika stiglo u bolnicu unutar 3 sata od nastupa simptoma akutnog moždanog udara, a 29 ih je u bolnicu primljeno više od 24 sata od nastupa simptoma. Spol nije imao značajnog utjecaja na vrijeme dolaska u bolnicu. Rezultati su pokazali kako većina bolesnika s akutnim moždanim udarom nije pristigla na hitni odjel unutar 3 sata od nastupa simptoma, što danas predstavlja vremenski okvir za trombolitičnu terapiju. Od ključne je važnosti utvrditi čimbenike koji su povezani sa zakašnjelim dolaskom u bolnicu. Opće prepoznavanje simptoma moždanog udara i shvaćanje važnosti ranog prijema u bolnicu neophodno je za poboljšanje rezultata dobivenih u ovoj studiji, u kojoj su glavne mjere ishoda bili vrijeme proteklo od nastupa simptoma do prijema u bolnicu i podobnost za trombolitičnu terapiju. Potrebna je daljnja izobrazba javnosti kako bi se povećala svijest o upozoravajućim znacima moždanoga udara.

Ključne riječi: Cerebrovaskularne bolesti – terapija; Cerebrovaskularne bolesti – dijagnostika; Akutna bolest; Hospitalizacija; Hitne medicinske službe – statistika i brožani podaci; Procjena invalidnosti