

MANAGEMENT OF PATIENTS WITH TRANSIENT ISCHEMIC ATTACK (TIA) AT SESTRE MILOSRDNICE UNIVERSITY HOSPITAL CENTER

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SUMMARY – Improved outcomes were observed in transient ischemic attack (TIA) patients after implementation of recommendations for stroke management and after multiple interventions such as public campaigns focused on raising awareness of stroke and reorganization of health services. The aim of this study was to describe reorganization of in-hospital services to improve the management of patients suspected of having TIA or stroke, and to validate these measures with patient outcomes. Data on 5219 patients examined between January 1 and December 31, 2008 at emergency neurology outpatient department were analyzed. Patients were referred by general practitioners, emergency physicians, or were brought by relatives without being previously seen by health services staff. The emergency services department is intended to improve care for TIA patients, providing a short standardized clinical assessment followed by initiation of a comprehensive stroke prevention program. Demographic data, risk factors, stroke type, previous TIA history, ABCD² scores and admission rates were analyzed. A total of 1057 patients suspected of having stroke or TIA were examined. There were 447 patients with ischemic stroke (mean age 73±11 years, 196 males) and 99 patients with TIA (mean age 67±14 years, 55 males). Parenchymal hemorrhage was diagnosed in 56 and subarachnoid hemorrhage in 49 patients, while 406 patients had nonspecific symptoms or other systemic or neurologic diseases. TIA preceded stroke in 29 (6.5%) patients and 197 (44%) patients were examined for worsening of stroke symptoms (133 within 24 hours, 47 within 48 hours, and 17 within 7 days). The mean ABCD² score was 2.95. In all examined patients, a comprehensive stroke prevention program was started; 427/447 (95%) strokes and 31/99 (31%) TIAs were hospitalized at neurology department. Four (4%) TIA patients developed stroke and were hospitalized, three of them after 2 days (ABCD² score 3.4 and 5) and one after 7 days (ABCD² score 5). Preventive measures resulted in a low number of strokes after TIA (<7%), but a relatively high percentage (44%) of stroke patients ignored initial symptoms and sought medical attention after persistence or worsening of the symptoms.

Key words: *Cerebral ischemia; Ischemic attack, transient; Cerebrovascular disorders; Stroke – prevention; Health education*

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Introduction

Stroke is still the most common cause of chronic acquired disability and the second leading cause of death in Croatia. Primary prevention measures have shown effects on reducing the stroke risk¹, but a statistically significant trend in stroke incidence rates over the past four decades showed a 42% decrease in stroke incidence in high-income countries and a greater than 100% increase in stroke incidence in low to middle income countries², and the same trend was evident in Croatia³. Despite evidence that thrombolytics improve outcomes after acute ischemic stroke⁴⁻⁶, still very few patients receive this treatment^{7,8}. The overall incidence of transient ischemic attacks (TIAs) is approaching that of ischemic stroke⁹, and TIAs precede up to a quarter of completed strokes¹⁰, thus giving clinicians an opportunity to avoid completed stroke and its devastating consequences. Patients with TIA are unstable; recent studies show that 4%-20% will have a stroke within 90 days after a TIA, half within the first 2 days¹¹⁻¹⁵. Although certain scores (ABCD, ABCD²)^{16,17} have recently been shown to be highly effective predictors of stroke risk, proper identification of patients at the highest and lowest risk of stroke in the first days and weeks after a TIA would require appropriate use of costly secondary prevention strategies. Treatments have been developed to prevent recurrent strokes at long term after a TIA or minor stroke¹⁸⁻²⁰. Appropriate interventions are predicted to reduce the long-term risk of recurrent stroke by as much as 80%-90%²¹. The guideline recommendations for admission to hospital²² after TIA are vague, and clinical practice is highly variable, with some institutions hospitalizing most of TIA patients and others none of them. There is substantial international variation in how patients with suspected TIA are managed in the acute phase. North American and UK guidelines²³ simply state that all patients in whom the diagnosis of TIA is suspected should be assessed and investigated within 7 days, yet this aim is frequently not achieved in practice. Services in European countries such as UK and France have been changed in the last five years by organizing TIA clinics or services for no-appointment assessment of patients with suspected TIA^{21,24,25}. Leaflets on TIA management and treatment were mailed to family doctors or primary care physicians to increase the awareness among community doctors of

the importance of early diagnosis, and to describe the service provided by the TIA clinic. Early initiation of the existing treatments after TIA or minor stroke was associated with an 80% reduction in the risk of early recurrent stroke.

In Croatia, recommendations for stroke and TIA management and treatment have been published^{19,26} and numerous preventive leaflets widely distributed. Public campaigns were focused on the awareness of stroke and TIA signs and symptoms, and the need to seek medical attention urgently. Studies on public awareness^{27,28} showed a moderate level of public knowledge of stroke warning signs and risk factors. About half of subjects correctly recognized more than half of stroke warning signs (at least 4 of 8) and risk factors (at least 7 of 14), and the majority of subjects would respond appropriately to stroke warning signs, meaning that they would seek immediate medical care. At the same time, a policy for emergency neurological evaluation of every patient seeking medical attention has been set, considering the previous general or emergency medical evaluation. In order to improve rapid assessment and treatment of TIA and stroke patients, healthcare services within the hospital have been reorganized, enabling 24-hour direct admission, diagnostic work-up and initiation of treatment.

The aim of the study was to describe the reorganization of in-hospital services to improve the management of patients suspected of TIA or stroke, and to validate the effect of these measures on patient outcomes.

Patients and Methods

Public campaigns focused on stroke risk factors and warning signs were conducted in parallel with focused symposia, workshops, educational courses and yearly updates on stroke and TIA management. Recommendations for the management of patients with stroke or TIA have been published¹⁹. In-hospital services have been reorganized to admit patients referred by general practitioners, emergency physicians, other specialists (internal medicine, ophthalmologist), or brought by relatives without having been previously seen by primary care physicians or other health care staff. The in-hospital service is intended to improve care for TIA patients, providing a short, standardized

clinical assessment followed by initiation of a comprehensive stroke prevention program. Clinical assessment was performed immediately by a neurologist trained in stroke management. If a TIA was suspected, further comprehensive tests were initiated. Brain imaging, non-contrast brain computed tomography (CT) scan was performed immediately at radiology department of Sestre milosrdnice University Hospital Center. Duplex ultrasonography (US) and transcranial Doppler (TCD) imaging of brain arteries to detect high-grade stenosis were done between 7 a.m. and 7 p.m. on working days. For patients seen after hours, the examinations were performed on the next morning. All vascular neurologists were fully trained in ultrasonography. Neurosonology examinations were performed to detect symptomatic high-grade carotid stenosis and enable carotid intervention, preferably carotid endarterectomy, within 2 weeks. Blood samples were tested for lipid profile, ionography, red blood cell, white blood cell and platelet counts, glucose concentration and creatinine. In patients with acute medical comorbidities, consultation with other specialists was performed. Patients at a high risk of stroke, with other medical comorbidities or complications, were admitted to the stroke unit. In patients at a high risk of recurrent embolism due to cardiac reasons, urgent echocardiography was performed.

TIA was defined as an acute loss of focal cerebral or ocular function with symptoms that lasted less than 24 hours and that were attributed to inadequate blood supply^{29,30}. Symptoms thought to be consistent with TIA were those defined by the ad hoc Committee established by the Advisory Council for the National Institute of Neurological and Communicative Disorders and Stroke³¹. Patients with incomplete recovery were judged to have a minor stroke. A stroke was defined by focal neurological deficit of sudden onset that lasted for more than 24 hours, with or without confirmation from brain imaging results.

We compared the risk of stroke in TIA patients at 30 days with that expected by using ABCD² score¹⁷. A seven-point score was calculated based on age (1 point for >60 years), blood pressure (1 point for $\geq 140/90$ mm Hg),

clinical features (2 points for unilateral weakness and 1 point for speech disturbance without weakness), diabetes (1 point) and duration of symptoms (1 point for 10-59 min and 2 points for >60 min).

Data on 5219 patients examined in the emergency neurological outpatient department during one year were analyzed. The local ethics committee approved the study. Demographic data, risk factors, stroke type, preceding TIA, ABCD² score, data on craniocervical artery disease and admission rate were analyzed. We evaluated the risk of stroke and death at 30 days in TIA patients using Kaplan-Meier method. The risk of stroke in TIA patients who developed stroke was analyzed separately.

Results

Between January 1 and December 31 2008, 1057 patients suspected of stroke or TIA were examined in the emergency neurological outpatient department. There were 447 patients with ischemic strokes, 99 with TIAs, 56 patients with parenchymal hemorrhages, 49

Table 1. Demographic data of 447 patients with ischemic stroke and 99 patients with transient ischemic attack (TIA)

	TIA patients	Stroke patients
Demographic data	N=99	N=447
Male, n (%)	54 (55.5)	196 (43.8)
Age (yrs, mean \pm SD)	67 \pm 14	73 \pm 11
Mean ABCD ² score	2.95	/
Pts that developed stroke after TIA (n/%)	4 (4)	29 (6.5)
Admission due to worsening of stroke symptoms	/	197 (44.1)
Risk factors	N (%)	N (%)
Hypertension	70 (77.8)	291 (65)
Diabetes mellitus	14 (14.1)	110 (24.6)
Hyperlipidemia	17 (18.2)	77 (17.2)
Atrial fibrillation	7 (7)	77 (17.2)
Craniocervical artery disease	26 (26.2)	79 (17.7)
Already taking aspirin	19 (19.2)	70 (15.6)
Already taking warfarin	5 (5)	31 (7)
Previous stroke	14 (14.1)	117 (26)
Previous myocardial infarction	6 (6.1)	56 (12.5)
Previous carotid intervention	3 (3)	9 (2)

Table 2. Admission of stroke patients due to worsening of stroke symptoms

Total admitted, N (%)	197 (44.1)
Admitted within 24 hours, n (%)	133 (29.7)
Admitted within 48 hours, n (%)	47 (10.5)
Admitted within 7 days, n (%)	17 (3.8)

patients with subarachnoid hemorrhages and 406 patients with nonspecific symptoms, other systemic or neurological diseases; 427/447 (95%) patients with ischemic stroke and 31/99 (31%) patients with TIA were hospitalized at University Department of Neurology. Demographic data of patients with ischemic stroke and TIA are summarized in Table 1. Table 2 shows admission rate of stroke patients. TIA preceded stroke in 29/447 (6.5%) patients, but 197 (44.1%) patients were brought to the neurology emergency room after worsening of stroke symptoms.

Demographic data on patients with TIA, risk factors and previous therapy are presented in Table 1. Hypertension was the most frequent risk factor (77.8%), and craniocervical artery disease was present in more

than a quarter of TIA patients (26.2%), with most of them having carotid disease, while only four patients had isolated vertebral artery occlusion without advanced carotid stenosis, and one patient was diagnosed with intracranial stenosis of the middle cerebral artery (Table 3). Out of 99 patients with TIA, 13 (13%) had symptomatic internal carotid artery stenosis.

Four (4%) TIA patients developed stroke within 30 days and were hospitalized later, three of them after 2 days (ABCD² score 3.4 and 5) and one after 7 days and 15 days (ABCD² score 5) (Fig. 1). Two patients had advanced carotid disease (two out of 26 TIA patients with craniocervical artery disease, 7.7%): one had left common and internal carotid occlusion, right internal carotid artery subtotal stenosis, and the other left internal carotid artery subtotal stenosis. The latter also developed recurrent stroke within 8 days of the previous stroke. None of the TIA patients died (Fig. 1).

Discussion

Despite the reorganization of in-hospital services enabling better management of patients with TIA, with a low rate of stroke (4% of patients seen in neu-

Table 3. Characteristics of craniocervical artery disease in patients with transient ischemic attack (TIA)

Carotid artery disease ipsilateral to affected arterial territory (symptomatic)	Carotid disease in the same patient contralateral to the symptomatic carotid stenosis (asymptomatic)	Vertebral artery disease
13 patients with subtotal internal carotid artery stenosis: 4 left, 9 right	2 patients with internal carotid artery occlusion 1 patient after stent placement 6 patients with mild to moderate carotid stenosis	2 patients with vertebral artery occlusion 2 patients with subclavian steal syndrome
2 patients after carotid endarterectomy, no restenosis	2 patients with mild to moderate carotid stenosis	
6 patients with moderate carotid stenosis		1 patient with vertebral artery occlusion
2 patients with mild carotid stenosis		1 patient with vertebral artery occlusion
2 patients with small plaques		2 patients with vertebral artery occlusion
1 patient without carotid disease but with middle cerebral artery stenosis		

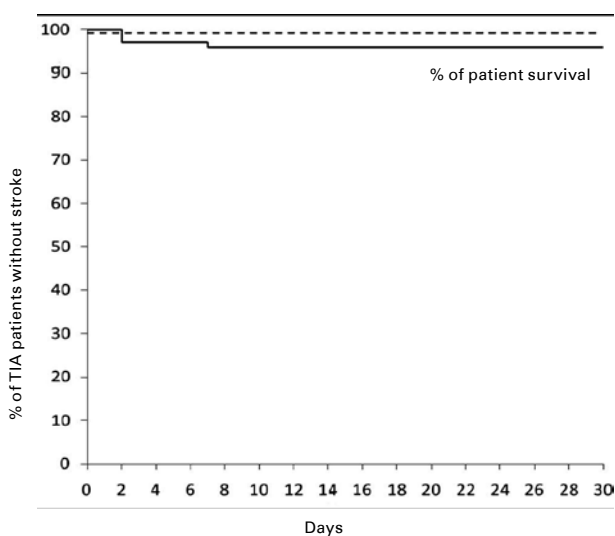


Fig. 1. Kaplan-Meier Life-Table analysis of survival free from stroke and death.

rological emergency room), our data showed that a high proportion (44%) of patients were examined and finally admitted to hospital after worsening of stroke symptoms. In a French study²⁵, SOS-TIA provided physicians with round-the-clock access to assessment, diagnosis, and immediate treatment for patients with suspected TIA. This study showed a very low rate of stroke within 90 days of TIA presentation (1.24% risk of stroke). The rate was lower than expected on the basis of the ABCD² score (5.96%). All strokes occurred in patients with definite TIA except for one, which occurred in a patient with a possible TIA. In the same study, patients with definite TIA and with a recent ischemic brain lesion had the highest risk of stroke (4.76%). The authors state that low rates were recorded despite the fact that three quarters of patients were discharged on the same day²⁵. In our study, the discharge rate was similar, as 69% of patients were discharged on the same day. However, four patients were later hospitalized due to the development of stroke. Three patients developed stroke after 2 days (ABCD² score 3.4 and 5) and one after 7 days (ABCD² score 5). Due to the small size of the cohort and limited statistical relevance (4 strokes within 30 days in 99 patients), we separately analyzed the risk factors in these four patients. Two of them had ABCD² score 5, which was associated with an increased stroke risk. In the OXVASC cohort of 188 patients¹⁶, only one stroke in patients with ABCD score less than 5

was recorded within 7 days, while the 7-day risk was 35.5% in those with ABCD score 6. Since the patient with the lowest ABCD score in the OXVASC cohort who had a stroke within 7 days had diabetes, a new ABCD² score was derived.

Two of four patients with TIA who developed stroke had advanced carotid disease and developed stroke despite medical treatment, one within 48 hours and the other one had the first stroke within 7 days and a recurrent stroke 8 days later. The 30-day stroke risk was high in patients with TIA and craniocervical artery disease (7.7%). Such results are consistent with the North Dublin TIA Study³². In this study that included 445 confirmed TIA cases, carotid stenosis predicted 90-day stroke (hazard ratio=2.56; 95% CI, 1.27 to 5.15, $P=0.003$). The risk of stroke rose with increasing grade of carotid stenosis, ranging from 5.4% (95% CI, 3.3% to 8.7%) with <50% stenosis to 17.2% (95% CI, 9.7% to 29.7%) with severe stenosis/occlusion (hazard ratio=3.3; 95% CI, 1.5 to 7.4, $P=0.002$). In the same group of TIA patients, the ABCD² score performed no better than chance for prediction of 90-day stroke, largely related to 24.2% of patients who experienced recurrent stroke and had low ABCD² score of 0-3. However, in 700 nonspecialist-suspected TIA cases, the predictive utility improved for stroke at 28 and 90 days. A higher rate of TIA was recorded in the group of patients with stroke: 6.5% had TIA preceding stroke, and an additional 44.1% of patients were brought to the neurology emergency room due to worsening of stroke symptoms (two thirds of them within 24 hours)³². Similar results were obtained in a population-based study of behavior immediately after TIA and minor stroke³³. In this study, approximately 70% of patients did not recognize their TIA or minor stroke symptoms correctly, 30% delayed seeking medical attention for >24 hours, regardless of age, sex, social class, or educational level, and approximately 30% of patients experienced an early recurrent stroke before seeking medical attention³³. This is probably the major reason for the low rate of therapeutic interventions in patients with stroke.

A high risk of stroke was recorded in patients with TIA and carotid stenosis. Although reorganization of hospital services enabled better access to the neurology emergency room and stroke and TIA management, low public awareness of stroke and TIA signs

still largely prevents successful management of such patients. Further public education of all demographic groups should be focused on proper recognition of TIA and stroke symptoms in order to enable full potential of acute stroke prevention and treatment.

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Sažetak

LIJEČENJE BOLESNIKA S PROLAZNIM ISHEMIJSKIM NAPADAJIMA U KLINIČKOM BOLNIČKOM CENTRU "SESTRE MILOSRDNICE"

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Zamijećen je poboljšani ishod bolesnika s prolaznim ishemijskim napadajima (TIA) nakon što su primijenjene preporuke za zbrinjavanje moždanog udara te nakon različitih intervencija kao što su bile javne kampanje usmjerene na podizanje svijesti o moždanom udaru i reorganizaciju zdravstvenih usluga. Cilj ovoga istraživanja bio je opisati reorganizaciju bolničke službe za poboljšanje liječenja bolesnika kod kojih se sumnjalo na postojanje moždanog udara ili TIA i provjeriti valjanost ovih mjera na ishodu bolesti. Analizirani su podaci o 5219 bolesnika pregledanih između 1. siječnja i 31. prosinca 2008. u hitnoj neurološkoj ambulanti. Bolesnici su bili upućeni od liječnika opće medicine, liječnika hitne medicinske pomoći ili su dovezeni u pratnji rodbine bez prethodnog pregleda osoblja u zdravstvenoj službi. Hitna neurološka službe je organizirana tako da poboljša skrb za bolesnike s TIA, te da pruži kratku i standardiziranu kliničku procjenu i pokrene sveobuhvatni program prevencije moždanog udara. Analizirani su demografski podaci, čimbenici rizika, tipovi moždanog udara, prethodne epizode TIA, zbroj ABCD² te stope prijma. Ukupno je pregledano 1057 bolesnika kod kojih se sumnjalo na dijagnozu moždanog udara ili TIA. Bilo je 447 bolesnika s ishemijskim moždanim udarom (srednja dob 73±11 godina, 196 muškaraca), 99 s TIA (srednja dob 67±14 godina, 55 muškaraca). Parenhimatozna krvarenja su dijagnosticirana kod 56, a subarahnoidno krvarenje u 49 bolesnika, dok je 406 bolesnika imalo nespecifične simptome ili druge sistemske i neurološke bolesti. TIA je prethodila moždanom udaru u 29 (6,5%) bolesnika, a 197 (44%) bolesnika je pregledano nakon pogoršanja simptoma povezanih s moždanim udarom (133 u roku od 24 sata, 47 u roku od 48 sati, a 17 u roku od 7 dana). Srednja vrijednost zbroja ABCD² je bila 2,95. U svih pregledanih bolesnika započeo je sveobuhvatni program prevencije moždanog udara, 427/447 (95%) bolesnika s moždanim udarom i 31/99 (31%) bolesnika s TIA je hospitalizirano u našoj Klinici za neurologiju. Četiri bolesnika s TIA su razvili moždani udar (4%) i bili hospitalizirani nakon toga, 3 bolesnika nakon 2 dana (zbroj ABCD² 3,4 i 5), a jedan nakon 7 dana (zbroj ABCD² 5). Preventivne mjere su rezultirale niskim brojem moždanih udara nakon preboljelog TIA (<7%), ali je relativno visok postotak (44%) bolesnika s moždanim udarom zanemario početne simptome i tražio liječničku pomoć nakon dužeg trajanja ili pogoršanja simptoma.

Ključne riječi: *Cerebralna ishemijska; Ishemijski napadaj; Cerebrovaskularni poremećaji; Moždani udar – prevencija; Zdravstvena izobrazba*

