ORIGINAL

RISK FACTORS IMPACT ON THE LONG -TERM SURVIVAL AFTER ISCHEMIC STROKE

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Introduction: Stroke is the second or third cause on a mortality list, and all projections indicate that this will remain in the year 2020. Furthermore, stroke is a leading cause of disability. A number of risk factors have been shown to be associated with stroke: age, sex, hypertension, diabetes mellitus, smoking, history of cardiac diseases, and past history of transient ischemic attack.

Aim: To analyze the impact of risk factors on the survival rate within a period of five years after ischemic stroke (IS).

Patients and methods: In this study 613 patients were analyzed with a first ever ischemic stroke admitted at the Department of Neurology Tuzla, from January 1st 1997 to December 31st 1998. Data were collected from patients' medical records after they were admitted to the hospital. The final examination of patients, who survived IS, took place five years after stroke. Medical history was obtained and presence of risk factors was evaluated on the day of admission. Computed tomography (CT) of the brain was performed for all patients during hospitalization. Ultrasonography of the supra-aortic trunks as well as electrocardiography has been performed to patients but this was not included in the study. The average age of patients was 65±10 (from 31 to 90) years, 333 (53%) were women. The most frequent risk factor was heart diseases which is registered in 525 (85.5%) patients, followed with history of hypertension in 419 patients (68%), cigarette smoking in 172 (28%), past history of transient ischemic attack in 168 (27%) and diabetes mellitus in 116 (19%). The risk factors were not registered in 1 (0.1%) patients.

Results: Five years after ischemic stroke 188 (31%) patients were survived. No statistical significance was occurred related to survival between men and women (p=0.4). The list number of patients who survived were over 70 years of age (19 or 10%), while the highest was between 41-50 years (30 or 60%). The average number of risk factors was 2.65±1.0 and significantly higher in men compared to women (2.7±1:2.3±1) (p<0.001). Significant difference was found in patients related to the existence of heart diseases (525 with compared to 88 without) (p <0.001), hypertension (with 419; without 194) (p<0.003), diabetes mellitus (with 116; without 497) (p=0.04) and cigarette smoking (with172; without 441) (p<0.001). Concerning transient ischemic attack there were no significant difference in survival in patients with ischemic stroke (p=0.7).

Conclusion: The survival rate after ischemic stroke was 31% within a period of five years. Long-term survival rate prognosis was significantly better in the younger patients, with no heart diseases, hypertension, and diabetes mellitus as well as in cigarette non-smokers.

Key words: ischemic stroke, risk factors, long-term survival

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INTRODUCTION

Stroke is the second or third cause on a mortality list, and all projections indicate that this will remain in the year 2020. Furthermore, stroke is a leading cause of disability. (1) Age and sex-standardized annual incidence of stroke is between 300-500/100 000 and stroke incidence is 16 to 35% greater in men than women. (2,3) The World Health Organization in the 1970's (4) define stroke as a "neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours". This definition was supposed to reflect the reversibility of tissue damage and was devised for the purpose, with the time frame of 24 hours being chosen arbitrarily. The 24-hour limit divides stroke from transient ischemic attack, which is a related syndrome of stroke symptoms that resolve completely within 24 hours. (5) Availability of early treatments can reduce stroke severity. There are some other prefer alternative concepts such as: brain attack and acute ischemic cerebrovascular syndrome. (6)

Stroke mortality varies greatly from country to country, aver-aging 50-100/100 000

per year in developed countries and 200-250/100 000 in Eastern European populations. (7) In the classifying (CVD) of cerebrovascular disease from the clinical point of view, it is most practical to have: ischemic stroke (IS), accounting for 70-80% of all strokes, intracerebral hemorrhage (ICH) (10 to 20% of the cases). (8) At the Department of Neurology, University Clinical Center Tuzla during a five-years post-war period (1996-2000) 2664 stroke patients were treated: 65% with IS, 25.5% with ICH, and 6.5% with SAH. Prior research in stroke prognosis focuses mainly on in-hospital and short-term mortality, but recently a few studies of the long-term prognosis after stroke have been published. (9,10,11) It is generally acknowledged that stroke is a multifactorial condition. (12,13,14) A number of risk factors have been shown to be associated with stroke: age, sex, hypertension, diabetes mellitus, smoking, history of cardiac diseases, and past history of transient ischemic attack. (15) However, their relative impact on the outcome of ischemic stroke varies from study to study and from population to population. Concerning this, only a few studies have been carried out in Bosnia and Herzegovina. The current study was undertaken to identify the importance of risk factors in outcome of ischemic stroke. Also, post-war period in Bosnia and Herzegovina with lack of medication, not regular medical follow up's made situation even worse to have proper prevention as well as treatment. The aim of this study was to analyze the impact of risk factors on the survival rate within a period of five years after first-ever ischemic stroke.

PATIENTS AND METHODS

We retrospectively analyzed 613 patients hospitalized for the first time due to ischemic stroke at Department of Neurology, University Clinical Center Tuzla from January 1st 1997 to December 31st 1998. All participants were consecutively recruited. Data were collected from patients' medical records. All patients in neurological exam had signs of stroke and they have been admitted at Department of Neurology, Division for Cerebrovascular Disease. Medical history was obtained and risk factors were evaluated at the day of admission. Only computed tomography (CT) of the brain was performed for all patients during hospitalization. Ultrasonography of the supra-aortic trunks as well as electrocardiography has been performed to patients but this was not included in the study. The history of previous stroke was excluding factor.

All patients were followed up until 5 year after their stroke when the final examination took place. We used the World Health Organization (WHO) definition of stroke as "rapidly developing symptoms and/or sign of focal, and at times global. Loss of cerebral function, with symptoms lasting more then 24 hours or leading to death with no apparent cause other than that of vascular origin". (16) Six hypothesized risk factors, namely hypertension, smoking, diabetes mellitus, history of hearth diseases and past history of transient ischemic attack were included in the study. History of hyperten-

sion was defined as systolic blood pressure over 140 mmHg, or diastolic blood pressure over 90 mmHg, or both diagnosed at least twice before the ischemic stroke or documented treatment of hypertension. History of heart disease (angina pectoris, myocardial infarction, atrial fibrillation, congestive heart failure) was accepted if it was diagnosed by a specialist of internal medicine or cardiologist. Diabetes mellitus was defined as use of a blood sugar lowering drug before the stroke onset or documented fasting blood glucose concentration exceeding 7.0 mmol/l. Smoking was considered as present when patients smoked daily previous to the stroke and absent when the patient had never smoked or stopped smoking for at least 1 year before the stroke onset. A history of transient ischemic attack (TIA) was defined when a patient had a temporary, focal neurological deficit presumably related to ischemia and lasing less than 24 hours, diagnosed by neurologist. The limitation of his study is that some other risk factors (hypercholesterolemia, stress...) have not been analyzed. After hospitalization surviving patients examined periodically, and final examination was performed 5 years after stroke. To evaluate which factors contribute to 5 year mortality, we compared the baseline characteristics for those patients who died within 5 years after stroke with those who not die within 5 years. Continuous and categorical data were analyzed using standard statistical test: mean value, t - test and X2 - test. Value of p<0.05 was considered to be significant.

RESULTS

Out of 613 patients with ischemic stroke, 188 (31%) patients survived five years. The annual mortality rate in patients with ischemic stroke was 13% for the second year and 4% to 6% for years through 5 years (Figure 1).
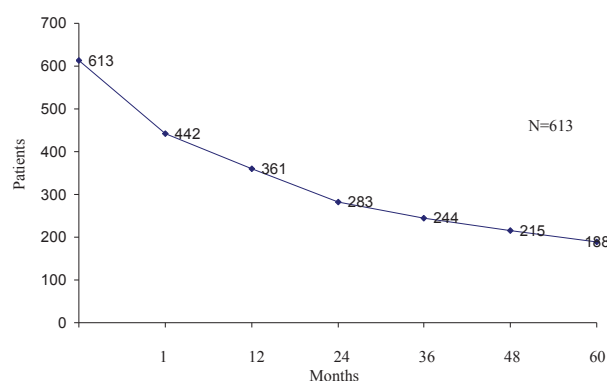

Figure 1. Five-year survival rate after ischemic stroke

The average age of patients with ischemic stroke was 65±10 years. The lowest number of patient that survived were over 70 years old (10%), while the highest number of survived was between 41-50 years (60%). The patients who died were significantly older than survived patients (68 +9.6: 63+9.3; p=0.005) (Table 1). Out of 613 patients, there were 278 men and 335 women. No statistical significance was occurred related to survival between men and women (p=0.4) (Table 2). In patients with ischemic stroke, the highest number

Table 1. Five-year survival rate after ischemic stroke according to the age

Survival rate (months)	Age 31-40		Age 41-50		Age 51-60		Age 61-70		Age >70	
	N	%	N	%	N	%	N	%	N	%
1	7	87.5	42	84.0	79	74.5	185	71.5	109	87.5
12	7	87.5	38	76.0	66	62.5	163	62.5	87	46.0
24	6	75.0	37	74.0	60	56.5	144	55.5	40	21.0
36	6	75.0	36	72.0	51	48.0	101	39.0	38	20.0
48	5	62.0	30	60.0	49	45.0	94	36.0	38	20.0
60	5	62.0	30	60.0	44	41.5	90	55.0	19	10.0

Table 2. Five-year survival rate after ischemic stroke according to the sex

Survival rate (months)	Men (N=278)		Women (N=335)		Total (N=613)	
	N	%	N	%	N	%
1	205	74.0	237	70.5	442	72.0
12	176	63.5	185	55.0	361	59.0
24	127	45.5	156	46.5	283	46.0
36	119	43.0	125	37.0	244	40.0
48	96	34.5	119	35.5	215	35.0
60	90	32.0	98	29.0	188	31.0

Table 3. Five-year survival rate after ischemic stroke according to the risk factors

Risk factors	Survived patients		Died patiens		p
	N	%	N	%	
Hearth diseases					
With (N=525)	140	27.0	385	73.0	<0.001
Without (N=88)	48	54.5	40	45.0	
Hypertension					
With (N=419)	114	26.0	305	74.0	0.003
Without (N=194)	74	33.0	120	67.0	
Diabetes mellitus					
With (N=116)	26	22.5	90	77.5	=0.04
Without (N=497)	162	33.0	335	67.0	
TIA					
With (N=168)	50	30.0	118	70.0	=0.7
Without (N=445)	138	31.0	307	69.0	
Smoking					
With (N=172)	75	43.5	97	56.5	<0.001
Without (N=441)	273	61.9	168	38.1	

of patients had two risk factors (37.3%), followed by patients with three risk factor (34.8%), then four (15.3%), one (8.6%), five (3.4%) and six risk factors (0.1%). One patient (0.1%) was without risk factors for ischemic stroke. The average number of risk factors according to sex was significantly higher in men (2.7 ± 1.1: 2.3 ± 1) (p<0.001).

The most frequent risk factor was registered in the patients with history hearth diseases in 525 (85.5%), then patients with hypertension in 419 (68%), smoking in 172 (28%), past history of transient ischemic attack in 168 (68%) and diabetes mellitus 116 (19%). Significant difference was found in patients related to the existence of hearth diseases (525 with compared to 88 without) and patients with cigarette smoking (172 with and 441 without) (p<0.001). Concerning transient ischemic attack there were no significant difference in survival in patients with ischemic stroke (p=0.7) (Table 3).

DISCUSSION

Ischemic stroke is interactions of the many risk factors and their influence to the outcome of ischemic stroke will be helpfull in understanding the complex epidemiology and etiology of stroke. This study shows significant association of five risk factors (hypertension, hearth diseases, diabetes mellitus, transient ischemic attack and smoking) and the survival rate within a period of five years after ischemic stroke. Five years after ischemic stroke 188 (31%) patients were survived. In our study mortality rate during first month was 28% and during first year 41%, decreasing over second (56%), third (60%) and fourth (65%) year after the stroke. However, in the study from central Italy, mortality one year after ischemic stroke was 36.9%. (17) Otherwise, Vemmos et al (18) reported 37% of mortality range one year after stroke. In study done by Arboix et al (2008) the in-hospital mortality rate was 12.9%. (19) Hankey et al (20) reported the cumulative risk of death five years after the first–ever stroke of 60% and annual risk of death of 10% between one and five years. Concerning mortality, the range in our study is somewhat higher than in other published papers. The fact that study was done few years after the war which had stressful impact to population could explain it. Bravata et al (21) followed 5123 patients with acute ischemic stroke, TIA, and carotid stenosis and found that patients with ischemic stroke had highest mortality after five year (60%). However, in the study Hardie et al (22), the authors analyzed trends in survival over five years after first-ever stroke for two cohorts of patients in 1989 - 90 and 1995-96. The 5 year cumulative risk of death was 59% and 58% respectively. No statistical significance was occurred related to survival between men and women (32%: 28%) (p=0.4). The lowest number of patient that survived were over 70 years old (10%), while the highest number of survived was between 41-50 years (60%). The age is the single most important factor for ischemic stroke. For each successive 10 years after age 55, the ischemic stroke rate more doubles in both men and women. (24) Our study implicates a significant role of cardiac diseases (85.5% with compared to15.5% without) (p<0.001). Hearth diseases and atrial fibrillation (AF) is the most powerful and treatable cardiac precursor of stroke. The incidence and prevalence of AF increase with age. With each successive decade of life above age 55, incidence of AF doubles. (23) Hypertension is the single most important modifiable risk factor for ischemic stroke. (16) Cigarette smoking is a significant risk factor in the present study (p=0.005). According to Benjamin et al. (1994) cigarettes smoking increases risk of ischemic stroke almost for a double. (24) In both the Framingham Study and the Nurses' Health Study (25,26) cessation of smoking led to a prompt reduction in stroke risk - major risk was reduced within two to four years. Statistical significance was occurred related to survival between patients with diabetes mellitus in the present study (p=0.04). Also, some other studies showed that the patients with diabetes mellitus have an increased susceptibility to atherosclerosis and an increased prevalence of atherogenic risk factors, notably hypertension, obesity, and abnormal blood lipids. Case-control studies of stroke patients and prospective epidemiological studies have confirmed an independent effect of diabetes with a relative risk of ischemic stroke in persons with diabetes from 1.8 to 3.0. Among Hawaiian Japanese men in the Honolulu Heart Program, those with diabetes had twice the risk of thromboembolic stroke of persons without diabetes that was independent of other risk factors. (27) In a population-based cohort in Rancho Bernardo, persons with diabetes had a risk-factor adjusted relative risk of stroke of 1.8 in men and 2.2 in women. In Framingham, persons with glucose intolerance have double the risk of brain infarction are other aspects of glucose metabolism that may play a role as a risk factor for ischemic stroke - specifically hyperinsulinemia and increased insulin resistance (the relative inability of insulin to enhance glucose disposal). Both were shown to be risk factors for ischemic stroke among subjects with normal glucose status. (28,29) In non - Hispanic white and Hispanic subjects, increased insulin resistance is associated with increased atherosclerosis of the carotid arteries independent of glucose status, insulin levels, and other major cardiovascular risk factors. (30) According to previous studies as well as in our study, the most important predictors for prognosis of long – term survival after ischemic stroke were age, heart diseases and smoking.

CONCLUSION

We found that stroke is associated with very high risk for death in acute and subacute phases. The survival rate after ischemic stroke was 31% within a period of five years. Long-term survival rate prognosis is significantly better in the younger patients, in the patients with no heart diseases, no hypertension, and no diabetes mellitus as well as in cigarette non-smokers. Better primary and secondary prevention, treating a stroke as a medical emergency, and management of acute stroke in "Stroke Unit" may improve the early and long-term survival rate and functional outcome.

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