Acta Clin Croat 2009; 48:399-403 Original Scientific Paper

RISK FACTORS AND OUTCOME DIFFERENCES BETWEEN ISCHEMIC AND HEMORRHAGIC STROKE

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SUMMARY – The aim of the study was to justify the hypothesis that risk factors do not differ between ischemic and hemorrhagic stroke. This retrospective study included 1066 stroke patients. The prevalence of risk factors and hospital-based survival were compared between patients with ischemic and hemorrhagic stroke. Data were retrieved from patient records. Statistical analysis was done by use of χ^2-test and t-test for dependent samples. The group of hemorrhagic stroke consisted of 70 (47.9%) female and 76 (52.1%) male patients. The group of ischemic stroke included 450 (48.9%) female and 470 (51.1%) male patients. Ischemic stroke patients had a higher prevalence of hypertension (79% *vs.* 72%), atherosclerotic diseases (50% *vs.* 34%) and atrial fibrillation (15.5% *vs.* 4.2%), and were statistically significantly older (72.5±10.4 *vs.* 65.7±12.8) than those with hemorrhagic stroke, however, fatal outcome was more common in the latter (26% *vs.* 17%). In conclusion, data analysis pointed to differences between hemorrhagic and ischemic stroke according to both risk factors and stroke outcome.

Key words: *Cerebrovascular disorders – classification; Cerebrovascular disorders – diagnosis; Cerebrovascular disorders – risk factors; Incidence; Age – distribution*

Introduction

Stroke is the second leading cause of mortality worldwide and remains the leading cause of adult physical disability. Almost 1 300 000 people die from cerebrovascular diseases in Europe every year. In 2007, some 6 million people died from stroke and millions suffer disabling sequels of stroke. The costs of stroke include medical care, rehabilitation and lost productivity of stroke survivors. It is measured in billions of euros every year. The costs in terms of pain and suffering of its victims and their families cannot be measured. Stroke is a highly heterogeneous disorder with distinct subtypes, each presenting specific clinical and epidemiological aspects[1,2]. Risk factors for stroke include systolic or diastolic hypertension, diabetes, atrial fibrillation, hypercholesterolemia, cigarette smoking, heavy alcohol consumption, and oral contraceptive use.

By definition, stroke produces neurologic deficits that persist for at least 24 hours. Stroke produces focal symptoms and signs that correlate with the area of the brain supplied by the affected blood vessel.

Ischemic stroke has many causes with different clinical presentations, risk factors, courses and outcomes[3,4]. The prognosis and management of ischemic stroke are directly related to the specific mechanism of ischemic lesion. Comparison of functional outcome and survival and recurrence rates can allow clinicians to identify patients at a higher risk of stroke recurrence and death. Early classification of ischemic stroke subtype is of substantial practical clinical value. The classification of ischemic stroke used in this study was The Oxfordshire Community Stroke Project (OCSP) classification, which defines four clinically identifiable subgroups of cerebral infarction: total anterior circulation infarction (TACI), partial

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Received October 27, 2008, accepted in revised form June 1, 2009

anterior circulation infarction (PACI), posterior circulation infarction (POCI), and lacunar infarction (LACI). OCSP has the ability to predict the prognosis and shows good correlation with the underlying pathophysiology and imaging findings on cranial computed tomography[5,6].

There is another stroke classification system used in some recent stroke studies, and it is named TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification, which denotes five diagnostic subgroups of ischemic stroke: large-artery atherosclerosis, cardioembolism, small-vessel occlusion, i.e. lacunar, stroke of other determined etiology, and stroke of undetermined etiology. One argument against the use of this type of subclassification system is the difficulty of performing the necessary technical examinations in all patients; so we decided to use OCSP in this particular survey.

Hemorrhagic stroke was classified as intracerebral hematoma or subarachnoid hemorrhage.

Correct classification of stroke subtypes in patients with acute stroke is crucial for early management and for predicting the prognosis[7,8].

The objective of this hospital-based study was to evaluate outcomes of patients with stroke (according to risk factors and stroke type) treated at Split University Hospital Center during a one-year period. The hypothesis was that ischemic and hemorrhagic strokes do not differ in outcome when risk factors are considered.

Patients and Methods

The study was retrospective and was conducted by three neurologists and two neurology residents. It included all patients treated for stroke at University Department of Neurology, Split University Hospital Center, Split, Croatia, during a one-year period (2006). Stroke was defined according to the World Health Organization definition as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting for more than 24 hours (unless interrupted by surgery or death), with no apparent cause other than of vascular origin"[9].

The study included first ever stroke, recurrent stroke, all ischemic strokes, and all types of hemorrhagic stroke as mentioned above. Recurrent stroke was defined as a new neurological deficit fitting the definition of ischemic stroke, occurring after a period of unequivocal neurological stability or improvement lasting for ≥24 hours and not attributable to edema, mass effect, brain shift syndrome, or hemorrhagic transformation of the incident cerebral infarction.

Medical chart of every stroke patient was surveyed for the following risk factors: sex, age, atherosclerotic disease, diabetes, hyperlipidemia, cigarette smoking, previous stroke, atrial fibrillation, and alcoholism, and for stroke outcome. The hospital-based study included 1066 patients.

Statistical analysis was performed using the Statistica 7.0 for Windows software, t-test for dependent samples and Pearson's χ^2-test. The level of significance was set at $P<0.05$.

Results

The study included 1066 stroke patients treated at University Department of Neurology, Split University Hospital Center, in 2006. Hemorrhagic and ischemic stroke are presented by subtypes in Table 1. There were 70 (47.6%) women and 76 (52.4%) men

Table 1. Stroke type and outcome analysis

	Outcome		
Stroke type	Incidence (%)	Deceased (%)	*P*
Intracerebral hematoma	111/146 (76.0)	37 (25.3)	
Subarachnoid hemorrhage	35/146 (24.0)	3 (2.0)	
Lacunar stroke (LACI)	153/920 (16.6)	22 (2.4)	
Partial anterior circulation infarction (PACI)	109/920 (11.8)	16 (1.7)	<0.001
Total anterior circulation infarction (TACI)	475/920 (51.6)	94 (10.2)	
Posterior circulation infarction (POCI)	183/920 (19.9)	24 (2.6)	

Table 2. Risk factor analysis

Risk factor		Stroke type		*P*
		Hemorrhagic (N=146)	Ischemic (N=920)	
Sex (n=546; 51.1%)	Male	76	470	0.753*
(n=520; 48.9%)	Female	70	450	
Age (yrs)	Mean ± SD	65.7±12.8	72.5±10.4	<0.001**
	Median	68	74	
	Range	28-93	35-95	
Hypertension (n=849; 80%)	yes	105	744	0.045*
Atherosclerotic disease (n=525; 49%)	yes	57	468	<0.001*
Hyperlipidemia (n=382; 36%)	yes	43	339	0.026*
Atrial fibrillation (n=153; 14%)	yes	7	146	<0.001*
Diabetes (n=465; 44%)	type 1	5	22	0.15*
	type 2	55	383	
Smoking (n=179; 17%)	yes	34	145	0.11*
Previous stroke (n=212; 20%)	yes	26	186	0.195*
Alcohol consumption (n=197; 18%)	yes	36	161	0.27*
Hospital stay (days)	Mean ± SD	11.9±8.2	10.9±11.6	0.84**
	Median	13	10	
	Range	1-39	1-31	

* χ^2 – test; ** t – test

Table 3. Risk factors according to stroke type and lethal outcome

	Risk factor	Deceased
Hemorrhagic stroke	Atherosclerosis	22/59 (37.3%)
	Smoking	5/34 (14.7%)
	Alcohol consumption	9/37 (24.3%)
	Atrial fibrillation	3/8 (37.5%)
	Previous stroke	7/27 (25.9%)
	Hyperlipidemia	9/44 (20.5%)
	Diabetes	17/62 (27.4%)
	Hypertension	37/127 (29.1%)
Ischemic stroke	Atherosclerosis	236/459 (51.4%)
	Smoking	17/142 (12.0%)
	Alcohol consumption	17/158 (10.8%)
	Atrial fibrillation	32/144 (22.2%)
	Previous stroke	34/182 (18.7%)
	Hyperlipidemia	37/331(11.2%)
	Diabetes	77/398 (19.3%)

with hemorrhagic stroke, and 450 (48.9%) women and 470 (51.1%) men with ischemic stroke. The mean age was 72.9±10.5 (range 33-95) years in female patients and 69.8±11.9 (range 25-94) years in male patients. Statistical analysis showed the women having suffered stroke to be significantly older than men (P<0.001). Risk factor analysis is presented in Table 2.

Atherosclerosis was more common in patients suffering from ischemic stroke than in those with hemorrhagic stroke. Atrial fibrillation and dyslipidemia were also more common as risk factors in ischemic than in hemorrhagic stroke. Patients with ischemic stroke were older than those with hemorrhagic stroke. Lethal outcome was more common in patients with hemorrhagic stroke, the difference being statistically significant (P=0.004). Table 3 shows differences in risk factors and lethal outcome between different types of stroke.

Discussion

Analysis and comparison of the data collected clearly showed the hemorrhagic and ischemic stroke

to differ according to some risk factors and outcome. Comorbidity has a significant impact on stroke outcome[10]. Prognosis depends on the type of stroke, the degree and duration of obstruction or hemorrhage, and the extent of brain tissue death. The location of hemorrhagic stroke is an important factor in the outcome, and this type generally has a worse prognosis than ischemic stroke. The 30-day mortality from hemorrhagic stroke ranges from 35 to 52 percent[11-15]; one-half of these deaths occur within the first two days[13,16]. Prognosis is generally poor when compared with ischemic stroke. Age, Glasgow Coma Score less than 8 at presentation, hematoma volume of greater than 60 mL, and intraventricular blood are predictors of high mortality[13,17,18]. Considering risk factors, atherosclerosis was more frequently found in ischemic stroke patients because atherosclerotic plaques narrow the inner diameter of the vessel, resulting in inadequate tissue vascularization.

Results of this hospital-based study confirmed that there was no sex difference in the type of stroke (P=0.753).

Considering risk factors for ischemic stroke, there is a consensus in population and hospital-based studies that hypertension is the most common risk factor predisposing patients for all subtypes of ischemic stroke. Our study confirmed this statement. Results of previous hospital-based studies suggest that ischemic stroke is a polyetiologic disturbance with clear differences in the risk factor profile among particular ischemic stroke subtypes. According to previous investigations, the synergistic action of hypertension, diabetes and hyperlipidemia predisposes patients for lacunar stroke[6]. Of the known controllable risk factors, hypertension is most important[19]. Hypertension accelerates the atherosclerosis process, thereby increasing the risk of atherothrombotic cerebral infarction. It also increases the risk of cerebral hemorrhage in part by promoting the development of cerebral vascular microaneurysms (Charcot-Bouchard aneurysms)[20,21].

Hemorrhagic and ischemic stroke differ according to outcome and risk factors. Atherosclerosis, atrial fibrillation and hyperlipidemia are the most powerful risk factors, which contribute to differences in manifestation of the resulting stroke type and outcome. These risk factors are by far more common in ischemic than in hemorrhagic stroke.

Ischemic stroke can be predisposed by excessive alcohol intake and by intracerebral and subarachnoid hemorrhage *via* multiple mechanisms (e.g., *via* hypertension, atrial fibrillation, rebound thrombocytosis and platelet aggregation and clotting disturbances)[22].

Our data confirmed the increased risk of primary intracerebral hemorrhage to be associated with low cholesterol, a relationship that may apply specifically to hemorrhages from hypertensive vasculopathy[23].

Since treatment measures for stroke are still rather limited, and knowing the high number of patients suffering stroke every year, it is important to be familiar with the stroke risk factor profile for each patient, and to be aware that prevention, i.e. timely identification and therapy for stroke risk factors, is the most efficacious method of stroke treatment. The individuals with a relatively high risk profile can take steps to modify other risk factors through lifestyle changes and/or medical treatment. Similarly, public awareness programs aimed at increasing the recognition of stroke warning signs and altering modifiable risk factors can be designed to address the high-risk groups.

Although this study did not produce any new or surprising results, the value of small hospital-based studies like this one lies in strengthening the awareness of the important role of stroke prevention while influencing risk factors. Every person, not only health care professionals, can contribute to stroke prevention by promoting healthy lifestyle and avoiding known risk factors for stroke.

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Sažetak

RAZLIKE U ČIMBENICIMA RIZIKA I ISHODU IZMEĐU ISHEMIJSKOG I HEMORAGIJSKOG MOŽDANOG UDARA

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Cilj studije bio je provjeriti opravdanost hipoteze kako se čimbenici rizika ne razlikuju između ishemijskog i hemoragijskog moždanog udara. Ova retrospektivna studija uključila je 1066 bolesnika s moždanim udarom. Učestalost rizičnih čimbenika i bolničko preživljenje uspoređeni su između bolesnika s ishemijskim i hemoragijskim moždanim udarom. Podatci su izvedeni iz bolesničkih kartona. Statistička analiza je provedena pomoću χ^2-testa and t-testa za zavisne uzorke. Skupina bolesnika s hemoragijskim moždanim udarom imala je 70 (47,9%) žena i 76 (52,1%) muškaraca, a skupina s ishemijskim moždanim udarom 450 (48,9%) žena i 470 (51,1%) muškaraca. Bolesnici s ishemijskim moždanim udarom imali su veću učestalost hipertenzije (79% prema 72%), aterosklerotske bolesti (50% prema 34%) i atrijske fibrilacije (15,5% prema 4,2%) i bili su statistički značajno stariji (72,5±10,4 prema 65,7±12,8) od bolesnika s hemoragijskim moždanim udarom, ali je smrtni ishod bio češći kod ovih potonjih (26% prema 17%). Dakle, analiza prikupljenih podataka ukazala je na razlike između hemoragijskog i ishemijskog moždanog udara u rizičnim čimbenicima i ishodu bolesti.

Ključne riječi: *Cerebrovaskularne bolesti – klasifikacija; Cerebrovaskularne bolesti – dijagnostika; Cerebrovaskularne bolesti – rizični čimbenici; Incidencija; Dob – raspodjela*