

## THE CHANGING INCIDENCE OF CEREBROVASCULAR DISEASE IN ZAGREB OVER A TEN-YEAR PERIOD

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**SUMMARY** – During the last decade Croatia was faced with war and population migration that entailed socioeconomic changes, modification of lifestyle, risk factors and health care, thus influencing the incidence and outcome of stroke. Data on patients admitted to University Department of Neurology in the years 1990 and 1999 were compared to estimate the incidence and prevalence of stroke and stroke subtypes, risk factors and outcome. In 1999, the number of stroke patients was almost twofold that recorded in 1990 and stroke patients were by 5 years younger. In 1999, there were more first-ever strokes (the incidence of crude first stroke increased by 57%), whereas the number of recurrent strokes increased in men and decreased in women. The proportion of ischemic stroke and subarachnoid hemorrhage did not significantly change, whereas parenchymatous hemorrhage increased in women. Hypertension was more common (83% versus 62%), whereas the prevalence of other risk factors did not change significantly. Patients were more often discharged for home care instead of rehabilitation center care. Mortality decreased in men and increased in women, whereas case fatality and crude mortality decreased leading to an increased stroke burden.

**Key words:** *Cerebrovascular accident – epidemiology; Cerebrovascular accident – mortality; Cause of death; Blood pressure – prevention and control; Risk factors; Croatia*

### Introduction

Stroke has been one of the major causes of death and disability in most countries for decades. There are many differences in disease occurrence, in terms of time, place, and each individual case<sup>1-6</sup>. During the 1950s and early 1960s, industrialized countries were characterized by increasing trends in stroke mortality. Lifestyle changes and reduction of risk factors in the mid-1960s and the next two decades were characterized by a slow but progressive decrease in stroke mortality<sup>7</sup>. During that period Croatia was in the group with East European countries that were characterized by an increase in stroke mortality, with a tendency of stroke incidence in younger age as the result of inferior socioeconomic circumstances<sup>1,2,8-10</sup>.

During the last decade Croatia became an independent state and was faced with the war, population migration and lifestyle changes, leading to an increase in the rate of stroke victims<sup>11</sup>. During the last few years stroke ranked as the leading cause of death in females in Croatia<sup>12,13</sup>. Stroke management has changed according to the current principles of stroke treatment<sup>13-15</sup>. This management is expected to increase the population aged over 60 in the next two decades<sup>16,17</sup>. The rising prevalence will thus lead to a greater stroke burden.

The aim of the study was to compare the following parameters between the years 1990 and 1999: general characteristics of stroke patients such as mean age, proportion of men and women, first stroke incidence, stroke prevalence, stroke subtype, frequency of conventional cardiovascular risk factors, and stroke outcome.

### Patients and Methods

Sestre milosrdnice University Hospital catchment area covers one fourth of the City of Zagreb and subur-

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ban areas with approximately 250,000 inhabitants (according to the last census, the population increased by some 50,000 inhabitants in the last decade). The policy of the University Department of Neurology is to admit all stroke patients presenting to the Neurology Emergency Room. Medical records of stroke patients admitted to Neurology Department in the years 1990 and 1999 were retrospectively evaluated.

The standardized work-up for stroke included blood hematology and chemistry, blood cholesterol and glucose levels, electrocardiography (ECG), chest x-ray, carotid and vertebral color Doppler flow imaging (CDFI) and transcranial Doppler (TCD), brain computed tomography (brain CT), angiography, and spinal tap with cerebrospinal fluid (CSF) analyses in selected patients.

The criterion for stroke (according to WHO criteria) was "rapidly developed 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 a vascular origin". By definition patients with transient ischemic attacks were excluded. The criterion for stroke classified as subarachnoid hemorrhage or intracerebral hemorrhage was verification of the clinical picture at brain CT or spinal tap. According to the International Classification of Diseases, Ninth Revision, patients were divided into three groups: ischemic stroke (code 434), parenchymal hemorrhage (code 431) and subarachnoid hemorrhage (code 430). Brain CT scans were performed in 86% of patients in 1990 and 89% in 1999. First stroke incidence was calculated as the rate of first stroke patients *per* 100 000 population; prevalence as the rate of all stroke patients *per* 100 000 population; mortality as the number of death cases *per* 100 000 population; and 28-day case fatality as

the proportion of death cases in hospitalized stroke population. Smoking habit and alcohol consumption were assessed by use of a questionnaire; those who confirmed regular or occasional cigarette smoking were considered as smokers, and those who confirmed regular alcohol consumption as alcohol consumers. Other conventional risk factors (hypertension, blood cholesterol, diabetes mellitus, heart diseases: cardiac decompensation, atrial fibrillation and myocardial ischemia) were assessed through the standardized work-up for stroke patients. Subjects who had systolic blood pressure  $\geq 140$  mm Hg or diastolic pressure  $\geq 90$  mm Hg, and subjects who reported treatment for hypertension were classified as hypertensives. Subjects who reported treatment for diabetes mellitus or subjects whose blood glucose level exceeded 6.7 mmol/L were considered to have diabetes. Blood cholesterol levels over 5.2 mmol/L were considered as elevated values. Heart diseases were diagnosed and confirmed by a cardiologist.

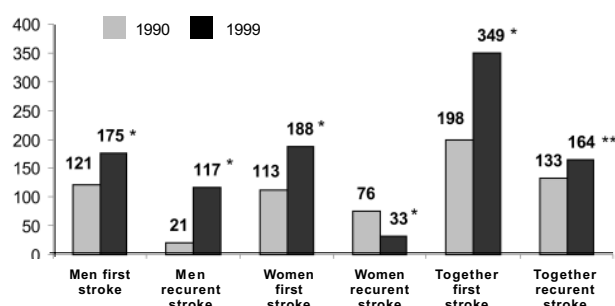
Data are presented as absolute number (expressed as mean  $\pm$  SD) and percentage. Statistical analysis was performed by the Statistica for Windows software (StatSoft Inc.). Proportions were used in most tables and figures, with  $\chi^2$ -test and Fisher's exact test to test differences in proportions. Statistical significance was set at  $p < 0.05$ ,  $p < 0.01$  and  $p < 0.001$ .

## Results

In 1999, the incidence and prevalence of stroke increased as compared to 1990 in both male and female (Table 1). In 1999, the number of stroke patients almost doubled in comparison with 1990 (1284 *versus* 662; the proportion of men and women did not change sig-

*Table 1. Number of stroke patients, mean age  $\pm$  SD, first stroke incidence, stroke prevalence and mortality in 1990 and 1999 (rate per 100 000 population)*

	No. of patients	Mean age $\pm$ SD	Incidence	Prevalence	Mortality
1990					
Women	378 (57%)	74.6 $\pm$ 16.3	113	189	38
Men	284 (43%)	72 $\pm$ 14.8	121	142	39
Total	662	73.3 $\pm$ 15.6	198	331	78
1999					
Women	731 (56%)	69 $\pm$ 15.1	176	292	38
Men	553 (44%)	67.3 $\pm$ 13.8	188	221	24
Total	1284	68.2 $\pm$ 14.5	349	513	66



\*  $p < 0.001$ ; \*\*  $p < 0.05$

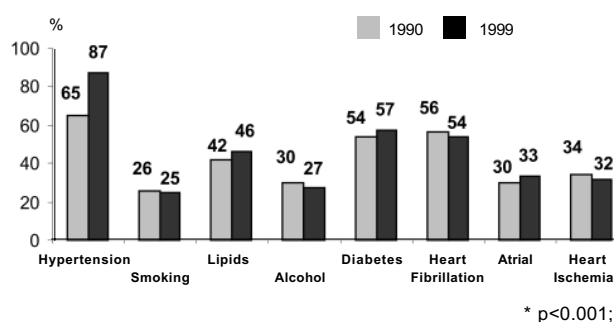
Fig. 1. Incidence of first and recurrent stroke events expressed as rates per 100 000 inhabitants in 1990 and 1999.

nificantly: 57% men in 1990 *versus* 56% in 1999;  $p > 0.05$ ). The mean age of stroke patients was by 5 years younger in 1999 (overall and sex specific). In 1999, the incidence of crude first stroke *per* 100 000 population increased by 57% as compared with 1990 (by 45% in men and by 66% in women;  $p < 0.001$ ). The prevalence (all stroke events) *per* 100 000 population also increased significantly: overall ( $p < 0.001$ ), and in both men ( $p < 0.05$ ) and women ( $p < 0.01$ ). In 1999, the overall crude mortality rate *per* 100 000 population decreased in comparison to 1990 ( $p < 0.05$ ) and in men ( $p < 0.05$ ) but remained constant in women ( $p < 0.05$ ).

The increase in the stroke incidence in 1999 as compared to 1990 was primarily due to the increase in first-

Table 2. Epidemiology of stroke in 1990 and 1999 according to sex and stroke subtype

	Ischemia	Parenchymal hemorrhage	Subarachnoid hemorrhage	28-Day case fatality
1990				
Women	315	61	7	75
%	83	16	2	20
Men	238	37	9	79
%	84	13	3	27
Total	553	98	16	154
%	83	15	2.4	23
1999				
Women	574	138	19	94
%	79	19	3	13
Men	456	80	17	62
%	82	15	3	11
Total	1030	218	36	156
%	80	17	2.8	14



\*  $p < 0.001$ ;

Fig. 2. Comparison of stroke risk factors between 1990 and 1999.

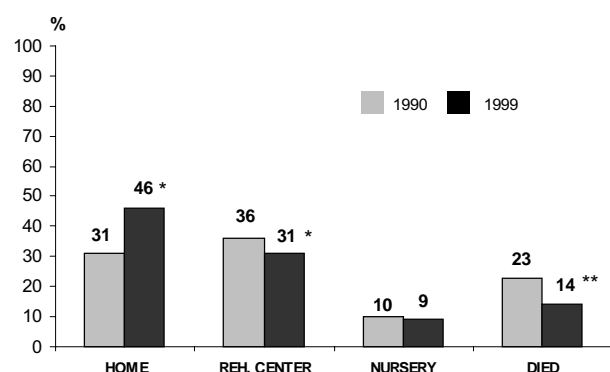
ever stroke (Fig. 1) (349 *versus* 198 *per* 100 000 population;  $p < 0.001$ ), and then to stroke recurrences (164 *versus* 133 *per* 100 000 population;  $p < 0.05$ ). There were more first-ever strokes in men (45% increase;  $p < 0.001$ ), whereas the number of recurrent stroke events increased 5.6 times ( $p < 0.001$ ). In women there were more first-ever strokes (66% increase;  $p < 0.001$ ) and less stroke recurrences (57% decrease;  $p < 0.001$ ).

There was no significant change between 1990 and 1999 in the overall proportion of ischemic stroke events (83% *versus* 80%;  $p > 0.05$ ) or according to sex (84% *versus* 82% in men and 83% *versus* 79% in women;  $p > 0.05$ ) (Table 2). Although the numbers are small, there was no significant change in the overall proportion of subarachnoid hemorrhage (2.4% *versus* 2.8%;  $p > 0.05$ ) or according to sex (3% *versus* 3% in men and 2% *versus* 3% in

women;  $p > 0.05$ ) (Table 2). There was no significant change in the overall proportion of parenchymal hemorrhage (15% *versus* 17%) and in men (13% *versus* 15%;  $p > 0.05$ ), whereas in women an increasing trend was observed (16% *versus* 19%;  $p < 0.05$ ) (Table 2). The 28-day case fatality decreased from 1990 to 1999 in both men and women (Table 2).

While hypertension significantly increased from 1990 to 1999 (by 22%;  $p < 0.001$ ), other risk factors showed no significant change (Fig. 2).

Comparison between 1999 and 1990 yielded a significant increase in the rate of patients discharged for home care (31% *versus* 46%;  $p < 0.001$ ), and a significant decrease in the rate of patients discharged to a rehabilitation center (36% *versus* 31%;  $p < 0.01$ ) (Fig. 3), whereas the rate of patients discharged to nursery



\*  $p < 0.001$ ; \*\*  $p < 0.05$

Fig. 3. Patient distribution according to hospitalization outcome in 1990 and 1999.

homes remained stable. The number of deaths also decreased (23% versus 14%;  $p < 0.001$ ) (Fig. 3).

## Discussion

In the year 1999, the rate of fatal stroke declined as compared to 1990 (13.2% versus 23%) both in men (11% versus 27%) and women (13% versus 20%). At the same time the incidence of stroke in 1999 was almost twofold that in 1990. The incidence of stroke in 1999 was 349 per 100 000 (188 in men and 176 in women), as compared to 198 per 100 000 (121 in men and 113 in women) in 1990. Such an increase in the rate of stroke was observed in Novosibirsk, Russia<sup>8</sup>, whereas the incidence was constant in industrialized countries, e.g., Rochester, Minnesota<sup>18</sup>.

The decline in the stroke mortality rates recorded in industrialized countries has been attributed to favorable trends in the hypertension detection, treatment and control<sup>19</sup>, and to advances in the diagnosis and treatment<sup>20-22</sup>. In our study the rate of hypertension increased by 20%, yet the 28-day case mortality decreased, being as low as in developed countries<sup>2,3,23</sup>. Although there was a speculation that improved diagnostic tools would directly influence the decline of mortality rates, the evidence for improved detection of mild events does not explain the observed improvement in survival. In a population-based study, Barker and Mullooly<sup>24</sup> found similar clinical manifestations of stroke with or without CT scans. Similar data have been reported from the Minnesota Stroke Survey<sup>25</sup>, when imaging studies were already in use in the 1980s, and improved survival rates were found in the subgroups of patients with notable deficits detectable without neuroimaging studies. Improved

survival rates have been suggested to be the result of a shift towards a reduced stroke severity<sup>24</sup>. Therefore the proportion of coma patients declined, whereas the proportion of stroke patients with speech or visual deficits increased between 1967 and 1985. The improvement in hypertension control<sup>24</sup> is thought to reduce the severity of incidence events. In the present study, the validation protocol did not discriminate among different levels of severity. The proportion of each stroke subtype (ischemic, parenchymal hemorrhage or subarachnoid hemorrhage) remained constant except for the rise in parenchymal hemorrhage in women. However, a 57% increase in the incidence of first-ever stroke (crude first stroke incidence) was observed in 1999, when the proportion of hypertension increased (21%). At the same time, the mortality rates decreased. The proportion of brain CT scans did not differ significantly (86% in 1990 versus 89% in 1999). Thus, the improved stroke survival rates could be explained by advances in the stroke management and treatment<sup>11,14</sup>.

The official mortality statistics is in good agreement only in some countries (western and northern Europe in MONICA), whereas in others it greatly underestimates or overestimates stroke mortality<sup>3</sup>. Applying the same criteria, mortality rate has shown a decline: expressed as crude mortality (66/100 000 in 1999 versus 78/100 000 in 1990) and as 28-day case fatality rate (13.2% in 1999 versus 23% in 1990). Crude mortality is thus approaching west European countries and United States<sup>26</sup>. In 1990, the 28-day case fatality rate of 23% (20% in women and 27% in men) was similar to that reported from Novosibirsk<sup>8</sup>, Italy<sup>27,28</sup>, and New Zealand<sup>7</sup>. The observed decrease in the 28-day case fatality rate from 23% in 1990 to 13.2% in 1999 was similar to the decrease observed in Rochester, Minnesota, where the rate decreased from 33% to 17% during the periods from 1945 through 1949 and from 1980 through 1984<sup>23,29</sup>. These data are consistent with the results from other studies<sup>30</sup>. Although hospital policy of all stroke admittance did not change, our study was biased. The survey was retrospective, thus limiting the comparison between 1990 and 1999. In addition, the study was hospital-based and only limited information could be obtained on non-hospitalized fatal and non-fatal stroke cases in the population. In addition, limited information was obtained on the percentage of stroke victims presenting to the Neurology Emergency Room.

During the last decade, Croatia was faced with many socioeconomic changes, including the war, migration of

population, political instability and economic uncertainty. These changes influenced the main population characteristics through neglecting their own health, leading to inadequate risk factor identification and control. This is probably the explanation for the observed 20% hypertension increase, leading to the higher percentage of parenchymal hemorrhage (17%) than in west European countries (Erlangen 14%, Athens 15%)<sup>4,31</sup>. An almost twofold increase in stroke patients, with a shift towards younger age is also the result of inadequate risk factor identification. Socioeconomic changes are impossible to measure, however, they obviously play a role in the dramatic increase in the incidence of stroke<sup>2</sup>. These are initial results on the increase in the stroke incidence in Croatia. Although better stroke management<sup>14</sup> may play a role in reducing the case fatality rate, there is an urgent need of national data evaluation and longitudinal measurement of stroke incidence and case fatality rate. The increase of stroke incidence in parallel with the reduced case fatality leads to a rapidly increasing number of younger disabled stroke survivors, urging the initiation of actions aiming at the reduction of stroke risk and the need of health service restructuring.

## Conclusion

In 1999, the incidence of first-ever strokes was almost twofold that in 1990 and these patients were by 5 years younger; the proportion of ischemia and subarachnoid hemorrhage remained unchanged, yet the rate of parenchymal hemorrhage in women increased. In men, the number of recurrent strokes increased 5.6-fold. Hypertension increased by 20%, but there were no statistically significant changes in other risk factors. Mortality and case fatality were reduced and patients were more often discharged for home care instead to rehabilitation centers. Such an increase in the rate of younger stroke survivors leads to an increase in the stroke burden.

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### Sažetak

#### INCIDENCIJA CEREBROVASKULARNIH BOLESTI U ZAGREBU TIJEKOM PROŠLOGA DESETLJEĆA

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Tijekom prošloga desetljeća Hrvatska je bila zahvaćena ratnim zbivanjima koja su donijela mnoge političke, socioekonomske i kulturološke promjene. Promjena načina života svakako je utjecala na modifikaciju čimbenika rizika, pa tako i na incidenciju i ishod moždanog udara. U ovom istraživanju uspoređeni su podaci o incidenciji, prevalenciji, vrstama i ishodu moždanog udara kod bolesnika koji su primljeni na Kliniku za neurologiju tijekom prijeratne 1990. i poslijeratne 1999. godine. U 1999. godini bilo je skoro dvostruko više bolesnika, incidencija prvog moždanog udara porasla je za 57%, dok je broj ponovljenih moždanih udara porastao u muškaraca, a pao u žena. Udio ishemijskog moždanog udara i subarahnoidnog krvarenja nije se statistički značajno promijenio, dok je broj parenhimnih krvarenja kod žena porastao. Hipertenzija se javljala češće (83% naprama 62%), dok se zastupljenost drugih čimbenika rizika nije promijenila. Bolesnici su se u 1999. češće otpuštali na kućnu njegu nego na rehabilitaciju. Opća smrtnost i smrtnost u muškaraca je u 1999. godini pala, dok je kod žena bila u porastu.

*Ključne riječi: Cerebrovaskularni ispad – epidemiologija; Moždani udar – smrtnost; Uzrok smrti; Krvni tlak – prevencija i kontrola; Rizični čimbenici; Hrvatska*