Risk Factors Impact on the Long-term Survival After Hemorrhagic Stroke

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ORIGINAL PAPER
SUMMARY

Aim: To analyze the impact of risk factors on the survival rate within a period of five years after hemorrhagic stroke (HS). Patients and methods: In this study 303 patients were analyzed with a first ever hemorrhagic stroke admitted at the Department of Neurology Tuzla, from January 1st 1997 to December 31st 1998. Data were collected from patient’s medical records, whereas the final examination of all patients, who survived HS, 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 in all patients during hospitalization. The average age of patients was 62 ± 11 (from 31 to 90) years, 180 (59%) were women. The most frequent risk factor was hypertension, registered in 252 (83%) patients, followed by history of heart diseases in 182 patients (60%), smoking in 72 (23.8%), diabetes mellitus in 26 (8.5%), history of transient ischemic attack in 24 (8%) and alcohol intake in 13 (4.3%) patients. The risk factors were not registered in 22 (7.3%) patients. Results: Five years after HS 82 (26.7%) patients survived. No statistical significance was found in survival between men and women (p=0.2). The lowest number of patient that survived were over 70 years old (9%), while the highest number of survived was between 41-50 years (60.5%). The average number of risk factors was 2.5 ± 1.0 and significantly higher in men compared to women (2.7 ± 1.2: 2.3 ± 1) (p<0.001). Significant difference was found in patients with hypertension (n=252) (p<0.0001), alcohol intake (n=13) (p=0.0170), as well as in patients with diabetes mellitus (n=26) (p=0.005). Regarding other risk factors such as heart diseases, cigarette smoking and transient ischemic attack there were no significant difference in survival in patients with hemorrhagic stroke (p=0.2; p=0.7; p=0.8; retrospectively). Conclusion: We found that hemorrhagic stroke is associated with a very high risk for death in the acute and subacute phase. The survival rate after hemorrhagic stroke was 26.7% within a period of five years. Long-term survival rate prognosis is significantly better among the younger patients, without hypertension, alcohol intake and diabetes mellitus.

Keywords: hemorrhagic stroke, risk factors, long-term survival.

1. INTRODUCTION

Stroke is the third leading cause of death and the leading cause of disability in the United States. Hemorrhagic stroke (HS) represent 20% of all stroke cases and have a mortality rate of 40–50%. Hemorrhagic stroke, which includes intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), occurs in 71 000–77 000 persons annually in the United States (1). The mortality rate has been reported as 40–50% for these stroke subtypes, and survivors are often affected by significant morbidity (1,2). The definitions for ICH and SAH are adapted from the Classification of Cerebrovascular Disease III-1989 (3). ICH was defined as nontraumatic abrupt onset of severe headache, altered level of consciousness, or focal neurologic deficit that is associated with a focal collection of blood within the brain parenchyma, as observed on computed tomography (CT) or during autopsy, and is not caused by hemorrhagic conversion of a cerebral infarction. SAH was defined as the nontraumatic abrupt onset of severe headache or altered level of consciousness that is associated with blood in the subarachnoid space, as observed on CT or during autopsy, or a clinical history and examination consistent with SAH in which xanthochromia and increased red blood cells are found in the cerebrospinal fluid.

It is generally acknowledged that stroke is a multifactorial condition (4,5,6). A number of risk factors have been shown to be associated with stroke namely age, sex, hypertension, diabetes mellitus, smoking, history of cardiac diseases, past history of transient ischemic attack and alcohol intake. However, their relative contribution in the outcome of HS varies from study to study and from population to population. With this background and the fact that only a few studies carried out in Bosnia and Herzegovina have explored the extent of the problem, particularly in multifactorial enviroment, the current study was undertaken to identify the important risk factors contributing to the outcome of hemorrhagic stroke. The aim of this study was to analyze the impact of risk factors on the survival rate within a period of five years after hemorrhagic stroke.

2. PATIENTS AND METHODS

We retrospectively analyzed 303 patients hospitalized with hemorrhagic stroke at Department for Neurology, University Clinical Center Tuzla. Computed tomography (CT) scan of the brain was done for all patients during hospitalization. Patients with previous history of any type of stroke have not been included in the study. Six risk factors: hypertension, alcohol intake, smoking, diabetes mellitus, history of hearth diseases have been analyzed and past history of transient ischemic attack were included in the study. Hypertension was defined as systolic blood pressure over 140 mmHg, or diastolic blood pressure over 90 mmHg. 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 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 lasting less than 24 hours, diagnosed by neurologist. 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 Chi-square (X2) test. Value of p<0.05 was considered to be significant.

3. RESULTS

Out of 303 consecutive patients with hemorrhagic stroke, 81 (26.7%) patients survived five years. The highest mortality rate was during first month (56%) and first year (59.5%), while this rate decreased during second (64%), third (69%) and fourth (70.5%) year (Figure 1).

The average age of patients with
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Hemorrhagic stroke was 62.0 ± 11 years. The lowest number of patient that survived were over 70 years old (9%), while the highest number of survived was between 41-50 years (60%) (Table 1).

Out of 303 patients, 123 were men and 180 women. No statistical significance was found related to survival between men and women (p=0.4) (Table 2).

In patients with hemorrhagic stroke, the highest number of patients had two risk factors (42.2%), followed by patients with one risk factor (24%), then three (16.5%), four (6.6%) and five (3.3%) risk factors. Twenty-two patients (7.3%) were without risk factors for hemorrhagic stroke. The average number of risk factors according to sex was significantly higher in men (2.7 ± 1.1:2.3 ± 0.9) (p=0.001).

The most frequent risk factor was hypertension registered in 83%, then patients with history with heart diseases in 60%, smoking 23.8%, diabetes mellitus 8.5%, past history of transient ischemic attack in 8% and alcohol intake in 4.3%. Significant difference was found in patients with hypertension (252 compared to 51 without) (p<0.0001), alcohol intake (13 compared to 290 without) (p=0.0170) as well as in patients with diabetes mellitus (26 with and 277 without) (p=0.005). Concerning other risk factors such as heart diseases, cigarette smoking and transient ischemic attack there were no significant difference in survival in patients with hemorrhagic stroke (p=0.2; p=0.7; p=0.8; retrospectively) (Table 3).

4. DISCUSSION

Hemorrhagic stroke is a multifactorial condition, interactions among the risk factors and their influence to the outcome of hemorrhagic stroke. This will be helpful in understanding the complex epidemiology and etiology of stroke. The present study demonstrated significant association among six risk factors (hypertension, heart diseases, diabetes mellitus, transient ishaemic attack, alcohol intake and smoking) and the survival rate within a period of five years after hemorrhagic stroke.

Five years after hemorrhagic stroke 81 (26.7%) patients were survived. The highest mortality rate was during first month (56%) and first year (59.5%), while this rate decreased during second (64%), third (69%) and fourth (70.5%) year. The study of Vemmos et al (7) pointed out that mortality rate in first year after hemorrhagic stroke was 53.2%, while the study in Central Italy showed that mortality rate was 58.2% which is similar to our results (8). Mortality rate in second year was 14% and in following three years was about 5%. Concerning our study and study made by Hankey et al (9) showed that patients who survived first month after hemorrhagic stroke had better prognosis for long-term survival. Stroke is generally more severe in patients with hemorrhagic stroke. Within the first 3 months after stroke, hemorrhagic stroke is associated with a considerable increase of mortality, which is specifically associated with the hemorrhagic nature of the lesion (10).

No statistical significance was found related to survival between men and women (p=0.4). The lowest number of patient that survived were over 70 years old (9%), while the highest number of survived was between 41-50 years (60%). The age is the single most important factor for hemorrhagic stroke. For each successive 10 years after age 55, the hemorrhagic stroke rate more doubles in both men and women (11).

The present study demonstrated

![Figure 1. Five-years survival rate after hemorrhagic stroke](image)

<table>
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<th>Survival rate (months)</th>
<th>Age (31-40)</th>
<th>Age (41-50)</th>
<th>Age (51-60)</th>
<th>Age (61-70)</th>
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<td>33</td>
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TABLE 1. Five-years survival rate after hemorrhagic stroke according to the age

![Table 1](image)

TABLE 2. Five-years survival rate after hemorrhagic stroke according to the sex

![Table 2](image)
a significant role of hypertension (83% with compared to 17% without) (p<0.0001) in the outcome of hemorrhagic stroke. Studies in many countries have shown that high arterial blood-pressure is the most important risk factor for HS in both sexes, in many different races, and irrespective of whether other risk factors are present or not (12).

The higher level of either systolic or diastolic pressure in middle age, the higher is the risk of stroke in later years. This applies equally to cerebral infarction or intracerebral hemorrhage. The present study findings correlate with earlier studies showing association of hypertension and hemorrhagic stroke (13,14,15). Lin et al (16) in a 16-years follow-up study of 16491 citizens of Hiroshima and Nagasaki concluded that elevated systolic and diastolic blood pressure was closely associated with hemorrhagic stroke.

Studies showed that hypertension is a significant and independent risk factor for ICH and SAH (17,18), Treatment of hypertension demonstrated the most important factor in reducing the incidence of hemorrhagic stroke as well as decreasing the risk of cardiovascular disease (19,29).

Hypertension accounts for 35-50% of hemorrhagic stroke risk, while patients with diabetes mellitus are 2 to 3 times more likely to develop stroke (21,22).

Little has been written about association of elevated blood glucose and hemorrhagic stroke. The present study findings correlate with earlier studies showing association of diabetes mellitus and hemorrhagic stroke. Melamed (23) showed a correlation between reactive hyperglycemia and HS and concluded the mortality was high in presence of hyperglycemia. In patients with cerebral hemorrhage, increased catecholamine release could cause an increase in blood-sugar, that is reactive hyperglycemia. Hyperglycemia then would be the epiphenomenon of hemorrhage, no bi cause. Patients with severe HS (Glasgow Coma scale (GCS) <9) and diabetes mellitus had an increased risk of death (HR 6.5;95% CI 4.68 to 8.90) compared with mild stroke(GCS>12) (24).

The association of high alcohol intake has been seen for all strokes, stroke deaths, cerebral infarction and hemorrhagic stroke (25,26). Current study findings also endorsed association between alcohol intake and hemorrhagic stroke; the association being significant for high alcohol intake (27). The present study demonstrated a non significant role in survival in patients with transient ischemic attack, heart diseases and cigarette smoking in the outcome of hemorrhagic stroke. According to previous studies as well as in our study, the most important predictors for prognosis of long-term survival after hemorrhagic stroke were older age, hypertension, alcohol intake and diabetes mellitus.

### 5. Conclusion

We found that hemorrhagic stroke is associated with a very high risk for death in the acute and subacute phase. The survival rate after hemorrhagic stroke was 26.7% within a period of five years. Long-term survival rate prognosis is significantly better among the younger patients, without hypertension, alcohol intake and diabetes mellitus.

### References

9. Hankey GL, Jamrozik K, Broadhurst
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Klaus Kaee Andersen, MS, PhD; Tom Skyhøj Olsen, MD, PhD; Christian Dehlendorff, MS Lars Peter Kammersgaard, MD. Hemorrhagic and Ischemic Strokes Compared. Stroke, 2009;40:2068-72.


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