

# The Impact of Modifiable Risk Factors on the Short-term Outcome of Stroke

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**Objective:** The high stroke morbidity and related mortality in Central-Eastern European countries might be related to several factors. In this study we used a large, database from Tîrgu Mureş (Romania) to investigate the impact of risk factors on the short-term outcome of stroke. We opted for this method as hospital databases usually provide more detailed information on risk factors, stroke severity and correlated outcome than population based registries.

**Methods:** We analyzed the data of 1478 consecutively hospitalized stroke patients during a period of one year, regardless of the ward they were admitted to. We recorded risk factors, stroke severity and correlated with the short-term outcome (i.e. in-hospital outcome, assessed by Glasgow Outcome Scale) of stroke.

**Results:** Significantly more men and patients with a lower age than the European average were admitted. 26% of admitted patients had a previous cerebrovascular disease in their history. The prevalence of modifiable risk factors such as hypertension, diabetes, hyperlipidaemia, smoking, etc was higher than in other European countries. Overall case fatality was 10.4% and 75% of discharged patients had some degree of disability. Outcome at discharge was worse with higher systolic and diastolic blood pressure, increased heart rate, higher serum glucose, higher white blood cell count as well as decreased consciousness and increased age.

**Conclusions:** In this large hospital based database we found an alarming number of untreated and frequently aggregated risk factors. Our findings emphasize the role of modifiable risk factors as well as indicate major opportunities for more efficient stroke prevention.

**Keywords:** stroke, cerebrovascular disease, demographic analysis, risk factors, outcome

## Introduction

According to the WHO Global Infobase [1] stroke is the third leading cause of death both for women and men in the European region. The initial fatality rate reaches at least 15% in average [2]; also, approximately one third of the survivors will have a permanent disability [3]. Although a decreasing trend in stroke related mortality was observed in Western European countries starting from the 1970's this was delayed by almost a decade in most Eastern European countries [4, 5] and did not appear in Romania until the second half of the 1990's [6]. Even with this decrease stroke related mortality is still four times higher in Romania than the EU average (when comparing the age standardized stroke related mortality in the 0-64 year-old age group). The fact is that Romania has the second highest stroke related mortality rate from all countries of the European Union (the first being Bulgaria), both in women and men and in all age ranges [6].

The high stroke prevalence and related mortality in Central-Eastern European countries might be related to several factors, including: higher stroke incidence, more severe stroke or less effective care. Although attempts were made to create comparative studies involving several Central-Eastern European countries [7], only minor epidemiological data regarding individual countries [4, 8] were published.

In this study we used a large, hospital based database from Targu Mures (Romania) to investigate the impact of several risk factors on the short-term outcome of stroke.

## Methods

The methods used for this study has been described previously [4, 7, 9]. Briefly, we analyzed a large, hospital based database, the Mureş Stroke Database, in an attempt to determine the factors influencing the short-term outcome. The Mureş Stroke Database (MSD) contains the data of 1478 consecutively hospitalized acute stroke patient admitted to County Emergency Clinical Hospital Tîrgu Mureş during a period of 1 year. We prospectively collected almost 150 types of data (history, general physical and neurological examination, lab results, neuroimaging, etc); the methods of data collecting was described earlier [7]. All patients with a diagnostic of acute cerebrovascular disease were considered, regardless of the hospital ward they were admitted to. Stroke severity on admission was scored using the National Institute of Health Stroke Scale (NIHSS) [10]. The modified five-grade Glasgow outcome scale [11] was used to describe patient condition on discharge (0: no signs at discharge, 1: mild neurological signs, 2: moderate signs but independent, 3: severe signs, dependent on other person, 4: death in hospital). Descriptive statistics, nonparametric tests (Kruskal-Wallis with Gaussian approximation followed if appropriate by Dunn's multiple comparison test) and general linear model were applied for data analysis using GraphPad Prism 5.00 for Windows (GraphPad Software, Inc., San Diego, California, USA). Unless otherwise stated all values are given as mean±SD. A p value less than 0.05 was considered significant.

Table I. Stroke types

| Type                            | Patients in MSD (%) | Average NIHSS score |
|---------------------------------|---------------------|---------------------|
| Ischaemic stroke                | 79.5                | 9.9                 |
| Transient ischemic attack (TIA) | 1.5                 | 1.7                 |
| Intracerebral hemorrhage (ICH)  | 17.3                | 15.99               |
| Subarachnoid hemorrhage (SAH)   | 1.4                 | 11.4                |
| Fatal stroke                    | 10.4                | 20.4                |
| Non-fatal stroke                | 89.6                | 9.9                 |

## Results

### Brief description of demographic characteristics, risk factors and stroke types

From the 1478 patients two patients were excluded for associated neurological diseases. Out of the remaining 1476 patients 51.8% were men and 48.2% women; the average age was  $66.6 \pm 10.5$  years and  $69.5 \pm 10.9$  years respectively (significantly higher in women).

Patients and relatives were interviewed for previously known (before admission) risk factors. From all patients 78% were known to have hypertension, 12.4% diabetes, 8.5% peripheral arterial disease (PAD, significantly higher in men, 14.1% vs 4.9%), 10.7% arrhythmias with embolic potential (mainly atrial fibrillation) and 9.2% were considered obese (based on BMI criteria on admission). Also 23.5% reported regular alcohol consumption (significantly higher in men, 40.2% vs 6.8%) and 22.8% (significantly higher in men, 34.3% vs 11.3%) were smokers (both assessed only by self-reporting, severity based categories were created but are not presented in this paper). Hyperlipidemia (increased cholesterol and/or triglycerides) was diagnosed in 9.2% of all patients (established by laboratory values upon admission). We also examined the differences in prevalence of the above risk factors in Romania between admission and discharge. We found that the actual number of patients with blood pressure based on blood pressure criteria is significantly higher (94%, almost 16% of patients had no knowledge about this risk factor). The same pattern could be observed for diabetes (known 12.4%, actual percentage was 21.1%,  $p < 0.0001$ ), arrhythmias with em-

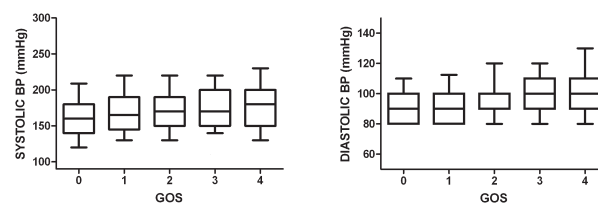


Fig. 1. Higher systolic and diastolic blood pressure on admission is associated with worse outcome (assessed by GOS, see Methods) Box and whiskers plot presents: mean  $\pm$  SD with whiskers at 10–90 percentile.

bolic potential (10.7% vs 13.1%,  $p = 0.02$ ), PAD (8.5% vs 14.9%,  $p < 0.001$ ) and hyperlipidemia (9.2% vs 43%,  $p < 0.0001$ ).

Around 26% of all patients from MSD had a previous stroke/TIA before the current event. The types of stroke and severity at admission is presented in Table I.

### Stroke outcome at discharge

Overall case fatality in hospital was 10.4%. Case fatality was different as function of the stroke type: 6.6% in ischaemic stroke and 26.9% in the case of ICH (significantly higher for ICH). The combined rate of death and dependency (GOS 3 or 4) was 26.7% in the case of ischaemic stroke and 58.3% in the case of ICH. The level of consciousness was reduced in 17.9% of ischaemic stroke patients whereas the same was true for 59.4% of patients with ICH. In general the severity of outcome was dependent on how severe the stroke was at the admission (see also Table I).

We analyzed the relationship of several factors on the short-term outcome including: distribution of age, level of consciousness, blood pressure, heart rate, serum glucose and also platelet and white blood cell count. Higher blood pressure (systolic and diastolic), increased heart rate, higher serum glucose, white blood cell (WBC) count as well as decreased consciousness and increased age were all associated with more severe outcome at discharge ( $p < 0.05$  in all cases, see also Figures 1–4).

In multivariate analysis case fatality was independently associated with increased age ( $p < 0.0001$ ), decreased level of consciousness at admission ( $p < 0.0001$ ), increased systo-

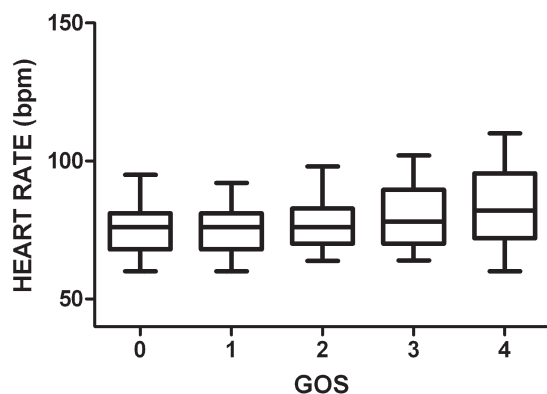


Fig. 2. Increased heart rate on admission is associated with worse outcome (assessed by GOS, see Methods) Box and whiskers plot presents: mean  $\pm$  SD with whiskers at 10–90 percentile.

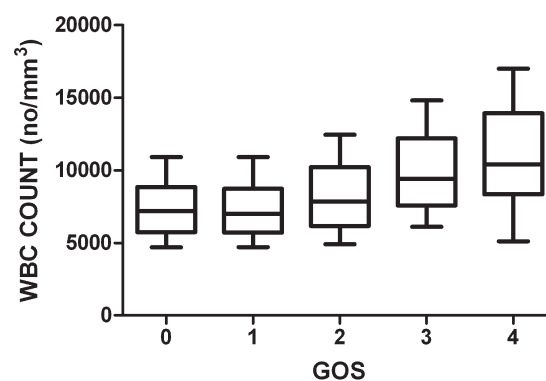


Fig. 3. Higher WBC count on admission is associated with worse outcome (assessed by GOS, see Methods) Box and whiskers plot presents: mean  $\pm$  SD with whiskers at 10–90 percentile.

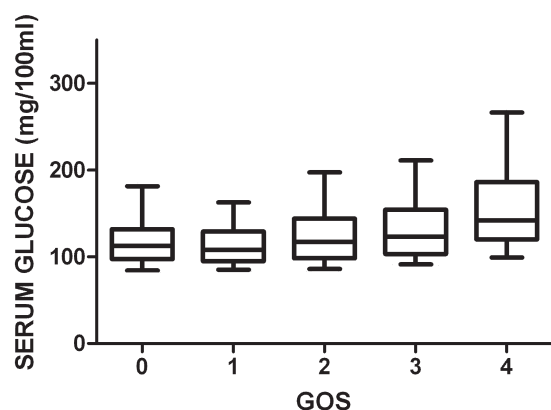


Fig. 4. Increased serum glucose level on admission is associated with worse outcome (assessed by GOS, see Methods) Box and whiskers plot presents: mean $\pm$ SD with whiskers at 10–90 percentile.

lic and diastolic blood pressure ( $p = 0.0002$  and  $p < 0.0001$ , respectively), increased heart rate ( $p < 0.01$ ), higher serum glucose level ( $p < 0.0001$ ), higher WBC count ( $p < 0.0001$ ), but not with platelet count ( $p = 0.0531$ ).

As the number of overlapping risk factors increases so did the probability of a fatal stroke ( $p < 0.05$ , see Figure 5).

## Discussion

Central-Eastern European countries had a high and even increasing mortality until the 1990's. Even though a delayed decreasing trend can be observed regarding the number of new stroke cases per year, as well as stroke mortality, Romania still struggles to overcome one of the highest mortality rates of stroke (second highest stroke related mortality rate from all EU member countries) [6]. In this paper we examined the impact of several risk factors on the short-term stroke outcome using a large, hospital based database.

The mean age of patients at stroke onset was lower by four years when compared to the European average [12]. This difference might be related to reduced life expectancy in Romania when compared to EU [6].

The ischaemic stroke type rate was similar with rates reported by previous European reviews [12,13] whereas the ICH was significantly more frequent. The overall fatality rate was comparable to averages from Europe [12] and other countries [3,14]. Interestingly the same was true for the stroke type specific fatality rates [15,16]; in comparison Hungary (another Central European country with high stroke mortality) reported a higher ICH fatality rate [4].

We found a worrying number of frequently overlapping risk factors. The prevalence of risk factors were higher than those reported in other countries.

The very high number of patients with hypertension is in concordance with previous studies in Hungary [4] but much higher than those reported in several other European countries [13] and the USA [17]. The high number of smokers is worrisome, especially because of the self-reporting method used; several studies proved the possibil-

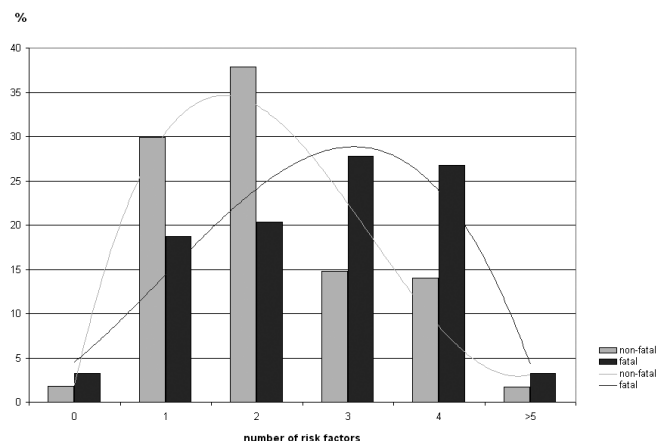


Fig. 5. Effect on short-term outcome of overlapping risk factors

ity of underestimation [18,19]. Also the high number of untreated hyperlipidaemic patients is problematic as there are several large studies showing its relationship with stroke [20,21]. Several proven risk factors had a high prevalence in the Romanian population with a trend to aggregation; but the most disturbing finding is the lack of knowledge and hence treatment of these risk factors. This is further emphasized by our multivariate analysis findings that prove the impact of these modifiable risk factors on the short-term stroke outcome.

The combined rate of death and dependency in the case of ICH is lower in our country than in Hungary but a much higher number of surviving ischaemic stroke patients are discharged in Romania with severe disability [4].

## Conclusion

Despite a younger age and the high number of (frequently aggregating) risk factors the overall short-term fatality rate is comparable in Romania with other European countries. Despite of this, because of the very high number of new cases stroke is still a leading cause of death. As such this study proves the efficacy of the in-hospital care in Mures County Emergency Hospital revealing in the same time the lacunas of the primary preventions system of the country. The high prevalence of modifiable risk factors prompts us again to emphasize the need of proper primary prevention as a proven cost-effective method. Possible suggestions to improve primary prevention include an increased awareness regarding the significance of the risk factors, the need to assess them periodically, a better compliance of patients regarding therapeutic measures and/or better medical community training. However because of the high number of recurring stroke patients the same principles should be applied to secondary prevention as well.

In our view the high number of patients with disability at discharge is a reflection of the impact of the risk factors on the outcome of stroke. This is especially worrying as 31.5% of the admitted stroke patients were still active (i.e. not retired) at the onset of stroke.

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