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# The clinical pattern of patients with recurrent stroke

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## Abstract

**Background:** Recurrent strokes account for about 25% of all strokes that occur annually. Studies show varying recurrence rates, ranging from 7% – 20% at 1 year to 16% – 35% at 5 years. Establishing a clinical pattern of patients with recurrent stroke could optimize the management strategy of this pathology.
**Material and methods:** A retrospective observational study was conducted that included 60 patients with primary stroke (n=30) and recurrent stroke (n=30). The severity of stroke was assessed using the National Institute of Health Stroke Scale scale and the degree of neurological disability – using the mRS scale. Predictive factors, post-stroke infectious complications and compliance with primary and secondary prophylaxis measures were also investigated. For the statistical analysis of the data, the Student's t test was performed for two independent samples.
**Results:** In the primary stroke group the mean age was 63.7±2.0 years, whereas in the recurrent stroke group it was 68.8±1.42 years. Statistically significant differences between groups were recorded for age (p=0.043), dyslipidemia (p=0.020), post-stroke infectious complications (p=0.032), cerebellar deficit (p=0.029), cognitive deficit (p=0.020) and neurological disability (p=0.003). Also, 93.33% of patients with atrial fibrillation following anticoagulant treatment as a secondary prophylaxis were under coagulated.
**Conclusions:** Elderly patients with poor risk factors control will be prone to experience a stroke of moderate severity, which will involve a moderate-severe degree of post-stroke disability, expressed by motor, sensitivity, verbal, cerebellar and cognitive deficit, as well as post-stroke infectious complications of the respiratory and urinary tract.
**Key words:** recurrent stroke, predictive factors, clinical pattern.

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## Introduction

Recurrent stroke is the onset of a repeated ischemic or hemorrhagic event in the brain, which lasts more than 24 hours and occurs after an initial stroke, regardless of the territory in which it occurs [1].

Recurrent strokes account for about 25% of all strokes that occur annually [2]. The incidence of stroke recurrence is high despite developments in primary and secondary preventive treatment [3, 4]. The cumulative incidence of stroke recurrence at 5 years varies between 16 and 30% in Western countries [1, 5–8]. Studies show varying recurrence rates, ranging from 7% – 20% at 1 year to 16% – 35% at 5 years [8, 9].

Stroke recurrence is closely and significantly related to increased mortality and morbidity [10, 11]. The risk of recurrence varies depending on the type of cerebrovascular disease and risk factors [12]. Risk factors for recurrent stroke are similar to those for primary stroke and include modifiable and non-modifiable factors.

The analysis of 30 studies suggests that hypertension is the main risk factor for recurrent stroke. During the period up to a recurrent stroke there is a number of changes in the cardiovascular system, including cerebral circulation such as vascular remodeling, inflammation, oxidative stress and baroreflex dysfunction, contributing to the pathogenesis of stroke in hypertension [13].

Age, diabetes, dyslipidemia and atrial fibrillation are other predictive factors for stroke recurrence, but they are presented in heterogeneous proportions in various studies [12].

Small vessels disease as compared to large artery atherosclerosis was associated with a lower chance of recurrence. Moderate level of evidence was found for a lower risk of an undetermined cause of stroke as compared to large artery atherosclerosis. No predictive imaging factors were found based on CT or ultrasound. A moderate level of evidence for the prediction of recurrent ischemic stroke based on MRI was found for multiple lesions, multiple stage lesions, multiple territory lesions, chronic infarcts, and isolated cortical lesions. A limited level of evidence was present for the association between white matter lesions and stroke recurrence [14].

The underlying mechanisms of stroke recurrence are not well known, and the etiology may be multifactorial. Epide-

miological and prospective studies have focused on predictive factors and the frequency of stroke recurrence, but not enough attention has been paid to this phenomenon on a case-by-case basis. Thus, the approach to the subject of predictability of stroke recurrence becomes complicated in the absence of a well-defined clinical pattern.

Elucidating the aspects related to the predictive factors of stroke recurrence in order to establish a clinical pattern of patients with recurrent stroke could optimize the management strategy of this disease.

## Material and methods

A retrospective observational study was conducted that included 60 patients with primary stroke (n = 30) and recurrent stroke (n = 30), admitted in the Stroke Unit of the Institute of Neurology and Neurosurgery of the Republic of Moldova in January 2019 – December 2019.

The inclusion criteria in the study were: patients with primary ischemic and hemorrhagic stroke and patients with recurrent ischemic and hemorrhagic stroke, confirmed by CT or MRI. The exclusion criteria from the study were: patients with ischemic and hemorrhagic stroke who died.

On admission stroke severity was assessed by NIHSS scale (National Institute of Health Stroke Scale), that is composed by 11 items and it is used to quantify the neurological deficit caused by a stroke. Thus, the NIHSS score between 0 – 4 points corresponds to a mild stroke, the NIHSS score between 5 – 15 points – to a moderate stroke, the NIHSS score between 16 – 20 points – to a moderate-severe stroke, and the NIHSS score between 21 – 42 points corresponds to a severe stroke.

The post-stroke infectious complications that occurred in these patients during hospitalization were also investigated.

The mRS scale (*modified Rankin Scale*) was used to measure the degree of disability or dependence in the daily activities of people who have experienced a stroke or other causes of neurological disability. This is an ordered scale from 0 to 6: a score of 0 points meaning no symptoms, and 6 points – the maximum score meaning dead.

Carotid Doppler ultrasound was used to identify the different degree of stenosis or vessels occlusion.

The following risk factors were investigated: hypertension (by stage), diabetes, dyslipidemia (according to total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides), smoking, cardiovascular disease (atrial infarction, myocardial infarction and valvular heart disease) and obesity (according to BMI).

For the statistical analysis of the data, the standard descriptive statistics kit was used through the data analysis of EXCEL and the Student's *t* test for two independent samples was performed on IBM SPSS Statistics 26.0. The use of the standard descriptive statistics kit facilitated the calculation of mean values and standard deviations, and the Student's *t* test for two independent samples allowed the calculation of the p value for each element investigated in this study.

## Results

The research included a total number of 60 patients with stroke – 33 women (55%) and 27 men (45%), the women:men ratio being 1.2:1. The mean age of the patients was 66.25±1.71 years, with limits between 44 and 92 years. Patients were divided into 2 groups as follows: the first group – 30 patients with primary stroke and the second group – 30 patients with recurrent stroke. Table 1 presents the general characteristics of study populations.

**Table 1**

**General characteristics of population study**

| Parameters | Primary stroke group | Recurrent stroke group | p |
|---|---|---|---|
| Age, years | 63.7±2.0 | 68.8±1.42 | <0.05* |
| Women, n | 18 | 15 | >0.05* |
| Men, n | 12 | 15 | >0.05* |
| Women:Men | 1.5:1 | 1:1 | >0.05* |

***Note:*** Statistical test applied: * - t Student for two independent samples.

In the primary stroke group the mean age was 63.7±2.0 years, unlike the group with recurrent stroke where the mean age was 68.8±1.42 years, which determined the presence of statistically significant differences between groups (p=0.043; p <0.05).

Regarding the sex criterion, in the primary stroke group the women:men ratio was 1.5:1, and in the recurrent stroke group the women : men ratio was 1:1 (p=0.44; p> 0.05).

The results obtained after the analysis of risk factors are shown in tab. 2.

**Table 2**

**Analysis of recurrent stroke risk factors/predictors**

| Parameters | Primary stroke group | Recurrent stroke group | p |
|---|---|---|---|
| Hypertension | - stage 1: 3.33%<br>- stage 2: 30%<br>- stage 3: 66.67% | - stage 1: 0%<br>- stage 2: 23.33%<br>- stage 3: 76.67% | 0.30<br>(p>0.05)* |
| Diabetes | 20% | 40% | 0.094<br>(p>0.05)* |
| Dyslipidemia | 26.67% | 40% | 0.020<br>(p<0.05)* |
| Obesity | - N/O: 73.33%<br>- class 1: 10%<br>- class 2: 10%<br>- class 3: 6.67% | - N/O: 56.67%<br>- class 1: 10%<br>- class 2: 23.33%<br>- class 3: 10% | 0.28<br>(p>0.05)* |
| Cardiovascular disease | - AF: 13.33%<br>- VHD: 3.33%<br>- MI: 6.67% | - AF: 36.67%<br>- VHD: 13.33%<br>- MI: 13.33% | 0.016<br>(p<0.05)* |
| Smoking | 26.67% | 33.33% | 0.58<br>(p>0.05)* |

***Note:*** AF – atrial fibrillation; N/O – Normal weight/Overweight; MI – myocardial infarction;
VHD – valvular heart diseas. Statistical test applied: * - t Student for two independent samples.

Regarding the severity of the stroke, moderate strokes were more common in both groups and there were no statistically significant differences between the NIHSS scores recorded in both groups of patients (10.1 points *vs* 11.7 points; p=0.17, p>0.05). The mRs score was of a statistically significantly higher average degree of disability (3.6 points *vs* 2.9 points; p=0.003, p<0.01) in patients with recurrent stroke, assigning a moderate-severe degree of neurological disability to these patients. The data are presented in tab. 3.

**Table 3**

**Assessment of stroke severity and neurological disability of patients**

| Parameters | Primary stroke group | Recurrent stroke group | p |
|---|---|---|---|
| NIHSS score | 10.1±0.78 points | 11.7±0.85 points | 0.17 (p>0.05)* |
| mRS score | 2.87±0.17 points | 3.57±0.15 points | 0.003 (p<0.01)* |

***Note:*** NIHSS – National Institute of Health Stroke Scale; mRS – modified Rankin Scale.
Statistical test applied: * - t Student for two independent samples.

Analysis of clinical data revealed that patients with recurrent stroke had a significantly higher proportion of cognitive deficit (20% *vs* 10%, p<0.05) and cerebellar deficit (30% *vs* 16.7%, p<0.05), as well as post-stroke infectious complications of the respiratory tract (29% *vs* 16.1%, p<0.05) and urinary tract (16.1% *vs* 6.5%, p>0.05). These results are shown in tab. 4.

**Table 4**

**Evaluation of patients clinical data**

| Parameters | Primary stroke group | Recurrent stroke group | p |
|---|---|---|---|
| Motor deficit | 90% | 96.67% | 0.30 (p>0.05)* |
| Sensitivity deficit | 63.33% | 63.33% | 1.0 (p>0.05)* |
| Visual deficit | 3.33% | 10% | 0.30 (p>0.05)* |
| Cognitive deficit | 10% | 20% | 0.020 (p<0.05)* |
| Cerebellar deficit | 16.67% | 30% | 0.029 (p<0.05)* |
| Aphasia | 46.67% | 60% | 0.30 (p>0.05)* |
| Pneumonia | 16.13% | 29.03% | 0.032 (p<0.05)* |
| Urinary tract infections | 6.45% | 16.13% | 0.078 (p>0.05)* |

***Note:*** Statistical test applied: * - t Student for two independent samples.

The evaluation of paraclinical data, namely the US Doppler examination found in patients with recurrent stroke a more advanced degree of atherosclerosis than in patients with primary stroke (53.3% *vs* 30.3%, p=0.069, p>0.05).

The level of compliance with the measures of primary and, especially, secondary prophylaxis was assessed, and in order to objectify the patients' words, the cases of patients with atrial fibrillation were investigated. Most often, in patients with atrial fibrillation/atrial flutter following anticoagulant treatment with vitamin K antagonists, INR should be between 2 and 3. Thus, of the 15 patients with atrial fibrillation, 14 (93.33%) had the INR<2 and only 1 patient (6.67%) had an INR between 2 and 3. Patients having an INR value < 2 get an insufficient dose of anticoagulant and thrombi can form in the heart cavities causing strokes. These results require a review of patients' risk factors control and of the gaps in the application of secondary stroke prevention measures. The data were plotted in fig. 1.

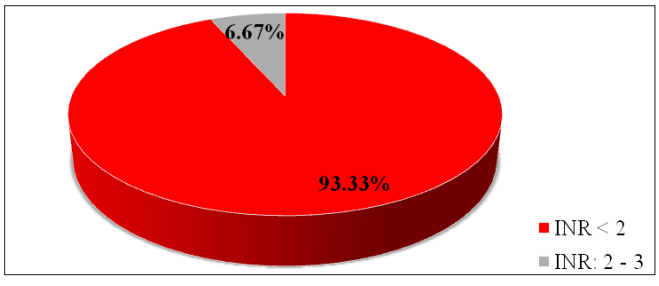


**Fig. 1. Control of coagulability by INR in patients with atrial fibrillation following anticoagulant treatment with vitamin K antagonists.**

Investigation of stroke recurrence predictors, as well as clinical and paraclinical data was the pivotal element of our research to establish a clinical pattern of patients with recurrent stroke. This was systematized in fig. 2.

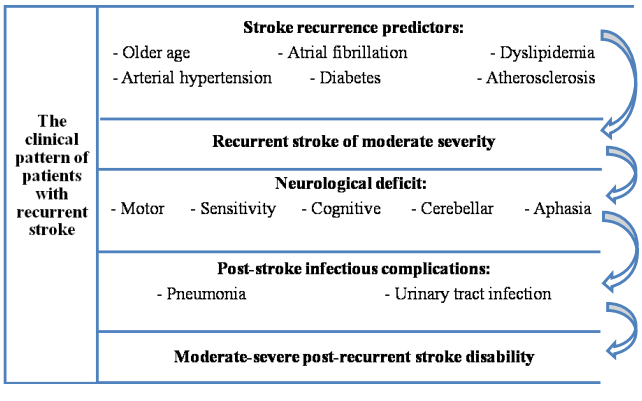


**Fig. 2. The clinical pattern of patients with recurrent stroke.**

## Discussion

The results of our study highlighted the following predictors of stroke recurrence: older age, persistence and/or progression of hypertension, diabetes, dyslipidemia, cardiovascular diseases(especially atrial fibrillation), advanced atherosclerosis and incorrect/inadequate risk factors control, confirming the data of other current papers [15-18].

The novelty of our research concerns the clinical aspects of recurrent stroke compared to those of primary stroke. The association of predictive factors and the newly discovered clinical elements allow shaping the clinical pattern of the patient with recurrent stroke. Regarding the stroke severity, moderate-grade strokes were more common in both groups. However, patients with recurrent stroke had a higher degree of disability than patients with primary stroke. Motor and sensitivity neurological deficits were registered with the same frequency in both groups of patients, but cognitive and cerebellar deficits were more common in patients

with recurrent stroke, their proportion doubling compared to that in patients with primary stroke. Currently there are no studies that integrate the clinical part of this disease.

It was observed that the majority of patients (93.33%) were exposed to the risk of recurrence of stroke due to non-compliance with secondary prophylaxis measures and inadequate/incorrect control of risk factors. A study assessing knowledge about risk factors in high-risk patients found that only 42% of patients with a history of stroke were aware of their own risk of recurrence and only 27% of them reported to their physician [19].

## Conclusions

Elderly patients with poor control of atrial fibrillation, dyslipidemia, stage 3 hypertension, diabetes mellitus and class 2–3 obesity will be prone to experience a stroke of moderate severity, which will involve a moderate-severe degree of post-stroke disability, expressed by motor, sensitivity, verbal, cerebellar and cognitive deficit, as well as post-stroke infectious complications of the respiratory and urinary tract.

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**Authors' contribution**
EM designed the study and revised the manuscript critically; MC collected the data, drafted the first manuscript. Both authors revised and approved the final version of the manuscript

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**Ethics approval and consent to participate**
No approval was required for this study

**Conflict of Interests**
The authors have no conflict of interests to declare