

## THE ISCHEMIC STROKE IN THE POSTERIOR CEREBRAL CIRCULATION

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### Abstract

*The purpose of the present study is to analyze the incidence of hemorrhagic transformation in the case of cerebral ischemic infarction of posterior cerebral artery in patients taking early post-infarction anticoagulants.*

**Key words:** ischemic stroke, posterior cerebral artery, hemorrhagic transformation, anticoagulants

### INTRODUCTION

The most common causes of posterior stroke are occlusion or embolism of major arteries, vertebrobasilar atherosclerosis or dissection and cardiac embolism (Savitz SI, Caplan LR, 2005; Caplan LR et al, 2004). Recent observational studies have shown an increased risk of stroke: three times for stroke after a transient ischemic attack of the posterior circulation or minor stroke in patients with spinal-symptomatic stenosis than in those without stenosis<sup>1, 2, 3</sup>. Extracranial vertebral artery dissection is also an important cause of stroke, especially in younger patients; it can be painless and usually occurs without a clear history of trauma. In a systematic analysis of vertebral artery dissection, the most common symptoms were dizziness or vertigo (58 %), headache (51%) and sore throat (46 %). The annual incidence of spontaneous vertebral artery dissection is estimated at 1-1.5 of 100 000 cases per year<sup>4</sup>. Less common causes include vasculitis and dolichoectasia (elongation) of vertebral and basilar arteries. In younger individuals, dolichoectasia may be an indication of Fabry disease, a rare inherited multisystem disease linked to lysosomal storage disorder<sup>5</sup>. Similar

<sup>1</sup> Gulli G, Marquardt L, Rothwell PM, Markus HS. Stroke risk after posterior circulation stroke/transient ischemic attack and its relationship to site of vertebrobasilar stenosis: Pooled data analysis from prospective studies. *Stroke* 2013;44:598-604.

<sup>2</sup> Gulli G, Khan S, Markus HS. Vertebrobasilar stenosis predicts high early recurrent stroke risk in posterior circulation stroke and TIA. *Stroke* 2009;40:2732-7.

<sup>3</sup> Marquardt L, Kuker W, Chandratheva A, Geraghty O, Rothwell PM. Incidence and prognosis of  $\geq 50\%$  symptomatic vertebral or basilar artery stenosis: prospective population-based study. *Brain* 2009;132:982-8.

<sup>4</sup> Schievink WL. Spontaneous dissection of the carotid and vertebral arteries. *N Engl J Med* 2001;344:898-906.

<sup>5</sup> Lou M, Caplan LR. Vertebrobasilar dilatative arteriopathy (dolichoectasia). *Ann N Y Acad Sci* 2010;1184:121-33.

to other forms of cerebrovascular and cardiovascular disease, the risk factors for strokes of the posterior circulation are hypertension, smoking, hypercholesterolemia, atrial fibrillation and coronary artery disease .

The use of HNF, HGMM or heparinoids for the treatment of a specific subtype of stroke or AIT can not be recommended due to lack of evidence. In patients with atrial fibrillation and AIT, oral anticoagulation with adjusted-dose of warfarin is the preferred therapy for preventing stroke. However, heparin is used by many such patients. The rate of bleeding complications in 7 days after heparinization is 10% with the massive bleeding rate of 2%.

Early recognition of posterior circulation stroke or transient ischemic stroke can prevent the onset of disability and save lives, but it is still difficult to recognize and effectively treat it than other types of stroke. Delayed or incorrect diagnosis and immediately delayed treatment can have devastating consequences, including death.

Assuming that hemorrhagic infarction or infratentorial cerebral hemorrhage secondary to a posterior ischemic cerebral infarction is a major problem affecting the early use of anticoagulants in patients with cerebral embolism, and some authors recommend early anticoagulation because of the increased risk of recurrent embolization in the first weeks after stroke, the purpose of this observational, prospective, group study is to monitor the clinical evolution of patients with posterior ischemic cerebral infarction early treated with anticoagulants.

## **MATERIAL AND METHODS**

This observational, prospective, group study was conducted in the Neurology Clinic in collaboration with the Radiology Clinic within the Emergency County Hospital from Oradea in the period 2011 - 2014, on a total of 55 patients hospitalized with the diagnosis of acute ischemic stroke in PAC territory.

The patients included in the study were patients with ischemic subtentorial stroke hospitalized within 24 hours after the onset without previous neurological history, aged between 18 and 80 years. Exclusion criteria were: patients with supratentorial ischemic stroke, onset of symptoms after more than 24 hours on hospitalization, presence of previous neurological history, age <18 years and > 80 years

To achieve a statistical study we developed a database processed in *Microsoft Office Excel 2010* in which we monitored: demographic information (age, sex), clinical and paraclinical evolution of patients on the severity of the neurological deficit with NIHSS scale, blood pressure,

etiology of brain injury, infarct location using the CT examination, the disease evolution under the anticoagulant therapy.

Through CT examination the following parameters were monitored: maximum size of the infarct area, calculated according to the formula maximum length x maximum width x number of slices of 1 cm 1: 2, the maximum space occupied by the perilesional edema the appearance of a visible hyperdensity in the infarction area as an expression of secondary hemorrhage, enhancement of the contrast substance, cortical and subcortical structures involvement in the infarction.

To assess the imagistic status, the ASPECT score was used, that uses brain CT images without contrast (native). All axial sections will be tracked and any early sign of cerebral ischemia will be considered.

Chi - square, Fisher's exact test were used as methods of statistical analysis, using the statistical software Medical MedCalc® (MedCalc® Software, Mariakerke, Belgium) version 12.2.1.0.

The study was approved by the Board of Internal approval of the research – development studies of the hospital and all patients or family first degree relative caregivers were asked to complete and sign an informed consent form after the risks and complications have been explained regarding the fibrinolytic therapy in acute ischemic stroke.

## RESULTS AND DISCUSSION

Comorbidities associated to stroke were hypertension, atrial fibrillation, carotid atheromatosis, obesity, type II diabetes and myocardial infarction, with statistically significant difference between the variables ( $p < 0.05$ ).

*Table 1*

***Comorbidities in patients with ischemic stroke in the ACP territory***

		Study group n=55	$p^{\dagger}$
Comorbidities	Myocardial infarction	2	$p < 0.0001^{**}$
	Diabetes type II	6	
	Obesity	9	
	Carotid atheromatosis	19	
	FIA	21	
	HTA	32	

$^{\dagger} p < 0.05$  shows a statistically significant difference between the studied groups; \* Fisher's exact test, \*\* Chi-square test

NIHSS score on arrival was divided into four categories of neurological severity: minor severity with NIHSS score between 1-4, mild

severity with NIHSS score between 5-15, moderate / severe severity with NIHSS score between 15 to 20, severe severity with NIHSS score between 20 – 25. Most of the patients were those with moderate to severe neurological status, followed by those with moderate, severe and minor neurologic status (Table 2).

ASPECT score showed a parenchymal hypoattenuation in most patients from both groups. Computer tomography was performed within 30 minutes of patient arrival into the hospital, not before it was monitored hemodynamically, glycemically, clotting sampling (platelets and INR) and urinary catheterization. The average weight was  $79.5 \pm 14$  kg, and the mean blood pressure was 162/82 mmHg. A normal brain CT has an ASPECT score of 10, while ischemic damage throughout the ACM has a score 0. In this study, all patients had an ASPECT score between 5-10 points (Table 2).

CT aspect highlighted an area of parenchymal hypoattenuation, or a deletion of intergyral spans suggesting an ischemic stroke being set. It may also reveal a constituted ischemic focus, focal edema or mass effect and normal aspect. Statistically, the normal aspect and the parenchymal hypoattenuation area prevailed, at a rate of 61.81%.

Table 2

*Clinical features in the patients under study*

		Study group n=55	$p^{\dagger}$
Average weight (kg)		79.5±14	
HTA (mmHg)	Systolic	162±19	
	Diastolic	87±14	
Glycemia mg/dl		152±56	
NIHSS Score	Minor 1-4	2	$p < 0.0001^{**}$
	Moderate 5-15	17	
	Moderate/Severe 15-20	24	
	Severe 20	12	
CT Aspect	parenchymatous hypoattenuation	9	$p < 0.0001^{**}$
	focal edema or mass effect	5	
	light deletion of gyrus in PAC territory	8	
	lesion formed in ACP territory	8	
	normal aspect	25	
ASPECT Score	0 - 5	5	$p < 0.000001^{*}$
ASPECT Score	5 - 10	50	

<sup>†</sup> $p < 0.05$  shows a statistically significant difference between the studied groups; \* Fisher's exact test, Chi-square test \*\*

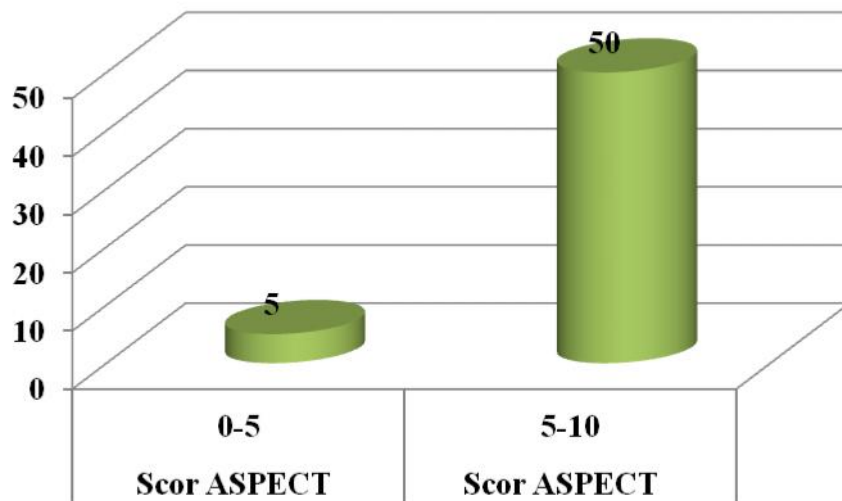


Diagram no. 1 Distribution of patients according to their neurological status at discharge from the hospital

The evolution of the neurological status was directly proportional to the time elapsed from the onset of posterior cerebral infarction to the arrival at hospital (Table no. 3).

Twenty-eight patients presented with installed neurological deficit under 3 hours from the onset, 24 patients at 3-6 hours after the onset, and 3 patients were evaluated neurologically at more than 6 hours after the onset.

Analyzing the evolution of the neurological status at admission in the hospital, we found that patients with moderate to severe NIHSS score prevailed in the early hours from the onset. Under anticoagulant and antiplatelet therapy, the evolution of the neurological status is favorable, especially in patients presenting within the first hours after the onset, when the ischemic lesion is in its early phase, and the neuronal death occurs in a small number of cells (Table no. 3).

Table 3

*Evolution of neurological status*

Time range (h)	Study group n=55	Value of NIHSS score at discharge	Number of patients	Value of NIHSS score at discharge	Number of patients	$p^{\dagger}$
< 3	28	1-4	2	1-4	8	<b>0.093269*</b>
		5-15	8	5-15	11	0.614843*
		15-20	13	15-20	6	0.128740*
		20	5	20	3	0.716092*
3 - 6	24	1-4	0	1-4	8	<b>0.005944*</b>
		5-15	7	5-15	9	0.787645*
		15-20	10	15-20	5	0.266166*
		20	7	20	2	0.161381*
6	3	1-4	0	1-4	2	0.495413*
		5-15	2	5-15	1	1.000000*
		15-20	1	15-20	0	1.000000*
		20	0	20	0	

$^{\dagger} p < 0.05$  shows a statistically significant difference between the studied groups; \* Fisher's exact test

The patients with posterior ischemic cerebral infarction early treated with anticoagulants had a post-treatment anticoagulant hemorrhagic transformation rate in a proportion of 30.9%, of which 7 (12.72%) patients died. Most of the patients had deep vascular coma highlighted imagistically by localized hemorrhage in the brain stem, the focus of ischemia or the cerebellar tentorium. Therefore, the average of NIHSS score was statistically significantly higher in these patients compared with those with favorable evolution. Of the latter, 25 were discharged home, and 16 were transferred to the neurological rehabilitation clinic (Table no. 4, Diagram 2).

Table 4

*Neurologic evolution at discharge from the hospital*

		Study group n=55	NIHSS score at discharge	$p^{\dagger}$
Hemorrhagic transformation	Discharged at home	5	15±6.59	$p < 0.0001^{**}$
	Transferred for recovery	2		
	Deceased	7		
Favorable evolution with home discharge		25	4.44±4.79	
Favorable evolution with transfer for recovery		16	11.875±3.05	

$^{\dagger}p < 0.05$  shows a statistically significant difference between the studied groups Chi-square test \*\*

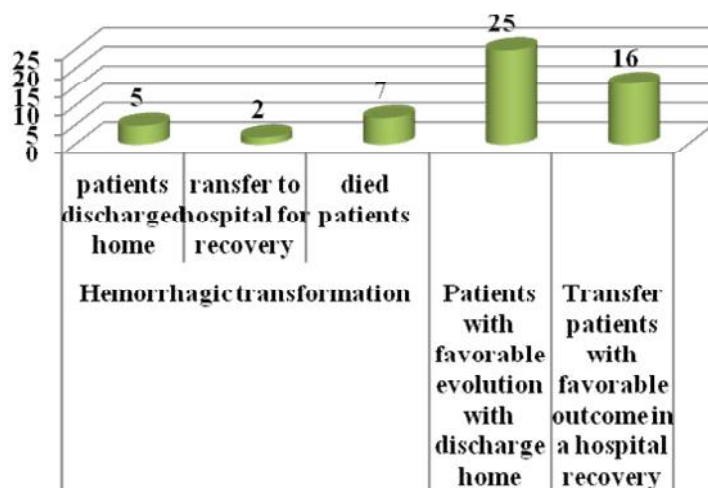


Diagram no. 2 Distribution of patients according to morbidity, mortality rate and neurological evolution at discharge from the hospital

**CONCLUSIONS**

Despite the data from the literature, which states that anticoagulant treatment is accompanied by an increased rate of hemorrhagic transformation of ischemic cerebral infarction, the present study demonstrates that anticoagulation in the early hours of the onset of

ischemia, under INR control and imaging, improved the neurological status of the patients with ischemic stroke.

The particularity of the study is that the PAC ischemic stroke may have a clinical at the onset that could mask the signs of ischemic focus. Therefore, a good history and neurological evaluation by NIHSS score combined with imaging assessment expressed by ASPECT score can accurately diagnose the neurologic injury and an early treatment avoids the installation of neurological disability and also of death.

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