

THE ROLE OF AUTONOMIC DYSFUNCTION IN OUTCOME OF STROKE PATIENTS

Entela Basha, Eris Ranxha, Olsi Taka, Vera Ostreni

Neurovascular Service, UHC "Mother Theresa", Tirana, Albania

Correspondence E-mail: bashaentela@gmail.com

Abstract

Introduction. Stroke is a major cause of morbidity and mortality in world and in Albania. Several studies have demonstrated that cardiac dysfunction may occur after vascular brain injury without any evidence of primary heart disease. During acute stroke, autonomic dysfunction elevated arterial blood pressure, atrial fibrillation, and ischemic cardiac damage, has been reported, which may worsen the prognosis. Autonomic disorders following a stroke can occur due to damage to brain regions that regulate the autonomic nervous system (ANS). The ANS controls involuntary functions such as heart rate, blood pressure, digestion, and thermoregulation.

Methods. We conducted a prospective study in Neurovascular Service. During 2023 in our service are been treated 1234 patients from 18 -102 years old. Patients with autonomic dysfunctions after stroke were included in our study were 126, 76 females and 50 males and who fulfilled all the criteria's study.

Discussion. The clinical relevance of autonomic nervous system imbalance after ischemic stroke is further confirmed in this study. We found that lability of arterial hypotension, arterial hypertension and heart rate variability may also predict an unfavorable outcome and dependency in post-stroke patients.

Conclusion. Effective management and early rehabilitation can improve outcomes, but persistent autonomic dysfunction may complicate recovery and increase mortality risk.

Keywords. stroke, autonomic dysfunctions, arterial hypotension, arterial hypertension, heart rate variability

ROLI I ÇRREGULLIMEVE AUTONOME NË ECURINË E PACIENTËVE ME AKSIDENTE CEREBRALE VASKULARE

Abstrakt

Hyrje. Aksidentet vaskulare cerebrale janë shkaku kryesor i sëmundshmërisë dhe vdekshmërisë në botë dhe në Shqipëri. Disa studime kanë treguar se disfunkioni kardiak mund të ndodhë pas një dëmtimi vaskular cerebral pa asnjë të dhënë për patologji primare kardiake. Gjatë aksidenteve vaskulo-cerebrale (AVC) ishemike akute, është raportuar disfunkcion autonom, hipertension dhe hipotension arterial, fibrilacion atrial dhe dëmtime ishemike kardiake, të cilat mund të përkeqësojnë prognozën. Çrregullimet autonome pas një AVC mund të ndodhin për shkak të dëmtimeve strukturore të trurit që rregullojnë sistemin

nervor autonom (ANS). ANS kontrollon funksionet e pavullnetshme si rrashjet e zemrës, presioni i gjakut, tretja dhe termorregullimi.

Metoda. Në Shërbimin Neurovaskular është realizuar në vitin 2023 një studim prospektiv mbi rolin e crregullimeve autonome në ecurinë e AVC ishemike. Gjatë një viti janë hospitalizuar 1234 pacientë nga mosha 18 -102 vjeç. Numri i pacientëve të përfshire në studim duke selektuar një kategori të vecantë pacientësh që nuk kanë faktorë konfondues që mund të ndikojnë në ndryshimin e rezultateve të studimit tonë ishin 126, 76 femra dhe 50 meshkuj.

Diskutimi. Rëndësia klinike e disfunksionit të sistemit nervor autonom pas AVC konfirmohet në këtë studim. Ne zbuluam se luhatjet e hipotensionit arterial, hypertensionit arterial dhe crregullimet e ritmit kardiak mund të parashikojnë gjithashtu një ecuri të pafavorshme në pacientët pas AVC.

Konkluzion. Menaxhimi efektiv dhe rehabilitimi i hershëm mund të përmirësojnë rezultatet, por mosfunkcionimi i vazhdueshëm autonom mund të komplikojë rikuperimin dhe të rrisë rrezikun e vdekshmërisë.

Fjale kyce: AVC, crregullime autonome, hipotensioni arterial, hypertensioni arterial, crregullime te ritmit kardiak.

Introduction

Stroke is a major cause of morbidity and mortality in world and in Albania. Several studies have demonstrated that cardiac dysfunction may occur after vascular brain injury without any evidence of primary heart disease (1,2). During acute stroke, autonomic dysfunction, elevated arterial blood pressure, arrhythmia, and ischemic cardiac damage, has been reported, which may worsen the prognosis (3,4,5). Autonomic disorders following a stroke can occur due to damage to brain regions that regulate the autonomic nervous system (ANS). The ANS controls involuntary functions such as heart rate, blood pressure, digestion, and thermoregulation. Disruptions in these functions can significantly impact recovery and quality of life post-stroke. Management focuses on stabilization and improving functional outcomes while addressing the risk of complications like sudden cardiac events. Increased or decreased blood pressure occur during acute phase of stroke. Post-stroke hypertension is common, and blood pressure lability may complicate recovery. Atrial fibrillation or other arrhythmias may arise due to stroke-related damage to autonomic centers.

Methods

We conducted a prospective study in Neurovascular Service due to 2023 in our service are been treated 1234 patients from 18 -102 years old. Patients including in our study with autonomic dysfunctions after stroke were 126, 76 females and 50 males.

1. The first-ever acute ischemic stroke,
2. Absence of diabetes mellitus or any other concomitant nervous system, cardiac that will affect the autonomic nervous system,
3. Absence of any clinically relevant arrhythmia on admission, including atrial fibrillation,
4. Absence of any pharmacological treatment, including beta-blockers, possibly affecting the autonomic nervous system,
5. Absence of any major concurrent illness, including renal failure and malignancies,
6. Absence of fever, hypoxia, severe hypertension, alterations in consciousness, or any relevant hemodynamic during the recovery.

All the patients were submitted to clinical, neurological, and functional examinations on 7th day and on 30 days after stroke. Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS), autonomy in activities of daily living (ADL) by the Barthel Index (BI), and global disability by the modified Rankin Scale (mRS) on day 7 and 30 after stroke. HVR measured with electrocardiogram monitoring on the 1-st, 7-th and 90-th day and electrocardiogram monitor

In order to limit confounding interactions, we decided to consider a homogeneous cohort of patients with acute first-ever ischemic stroke and without major cardiovascular and metabolic comorbidities. Patients with any form of structural heart disease, heart failure, atrial fibrillation and diabetes mellitus were preliminarily excluded, avoiding any possible effect on clinical outcome of stroke.

Results and discussion

A preserved autonomic balance represents one of the most relevant factors influencing post-stroke outcome. Activity of Living (ADL) and Barthel Index (BI) score was divided into 2 ranges (BI \geq 40 and <40). During the acute period (from onset to approximately 7 days), all patients with a BI \geq 40 and absence of autonomic disorders could improve their ADL in 30 days. Patients with a BI<40 and the presence of autonomic disorders exhibited two ADL recovery outcomes (improved and no change) at 30 days. (Tab.1) We also found that the skill level of basic activities related to standing was significant indicator of BI improvement. BI scores determined at approximately 1 week were reliable predictors of ADL disabilities at 1 month.

Table 1. NIHSS (National Institute of Health Stroke Scale), ADL (Activity of Daily Living), mRS (modified Rankin Score), BI (Barthel Index), HO (hypotension orthostatic), HA (Hypertension Arterial), HVR (Heart Rate Variability), LVO large vessel occlusion.



	Total N= 126	Favorable outcome	Unfavorable outcome	p value
Female	76 (60.3%)	50 (65.7 %)	26 (34.3%)	0.001
Ages	68±12.3	64±11.3	73±10.5	0.03
Male	50 (39.7%)	39 (78%)	11(22%)	0.03
Ages	66±11.3	64±12.4	68±12.6	0.01
Day 7				
NIHSS	7.6±10.3	6.8±6.5	8.4±5.6	0.04
ADL	3.5±2.1	4.2±1.1	2.8±1.9	0.02
mRS	2.4±1.9	2.1±1.1	2.9±1.9	0.02
BI	38±35.1	56±24.6	35±26.8	0.01
HO	33 (26.1%)	8 (0.6%)	25 (19.8%)	0.01
HA	54(42.8%)	21(16.6%)	33 (26.1%)	0.03
HVR	41 (32.5%)	8 (0.6%)	33 (26.1 %)	0.13
Day 30				
NIHSS	6.6±8.3	5.5±4.5	8.5±4.9	0.02
ADL	3.1±1.6	3.2±1.6	2.8±1.9	0.01
mRS	2.4±1.9	1.9±1.2	2.9±1.9	0.02
BI	38±35.1	46±21.6	35±18.8	0.03
HO	16 (12.6%)	6 (0.47%)	10 (0.79%)	0.01
HA	21 (16.6%)	8 (0.6%)	13 (10.3 %)	0.014
HVR	13 (10.3)	5 (0.39%)	8 (0.63%)	0.021
Stroke subtype				
Cardioembolic	31 (24.6%)	20 (15.8%)	11 (0.8%)	0.02
LVO	59 (46,8%)	41 (32.5%)	18 (14.2 %)	0,01
Un. Etiology	36 (28.5%)	21(16.6%)	15 (11.9%)	0.012

A major correlation between autonomic nervous system dysfunctions and cardiovascular morbidity in patients with heart disease has been consistently established in different clinical study, as confirmed by a recent review of the extensive available literature (8). Recent studies have shown that also in post-stroke patients there is an association between direct and derived measures of increased sympathetic activation and/or reduced vagal activity and a greater propensity for an adverse clinical outcome (9).

We found that age and severity of presenting neurological deficit, as assessed by currently clinical scales, have a major impact on rehabilitation outcome (7). We also observed that functional outcome was clearly affected by the presence of autonomic nervous system dysfunction, as expressed by a decreased or increased HRV (heart rate variability). In particular, patients with decreased HRV were more likely to experience an unfavorable outcome, even in the absence of any major comorbidity. The clinical relevance of autonomic nervous system imbalance after ischemic stroke is further confirmed in this study. In fact, we found that lability of arterial hypotension, arterial hypertension and heart rate variability may also predict an unfavorable outcome and dependency in post-stroke patients.

According to the findings, differences in the initial functional outcomes and recovery after follow-up were shown among the two groups. Differences were observed in all three functional outcomes, including ADL, mRS, BI. This result suggests that the severity of autonomic dysfunction influences the functional prognosis in patients with acute stroke. Additionally, when comparing the differences between the two groups, LVO group and cardio embolic group showed statistically differences. This indicates that functional recovery was more unfavorable in the LVO group. However, there was significant difference between the moderate and severe groups based on NIHSS, suggesting that autonomic dysfunction, HO, HA, HVR were more prominent in patients with high NIHSS, severe stroke. Autonomic dysfunction can lead to impaired functional outcomes for several reasons. First, symptoms due to autonomic dysfunction, including dizziness and orthostatic hypotension, can reduce the frequency and intensity of rehabilitation. Second, the dysregulation of the sympathetic and parasympathetic nervous systems can lead to insufficient blood supply to the injured brain tissue. Third, the autonomic nervous system is important for regulating stress and maintaining homeostasis in response to the brain's perception of stressors such as acute and chronic stroke (10). Fourth, autonomic dysfunction after acute stroke can lead to down regulation of cardiac function. According to a study by Scheitz et al., this phenomenon is called stroke-heart syndrome and is characterized by changes in cardiomyocyte metabolism, the deregulation of the leukocyte population, and vascular changes, which can lead to stroke-induced cardiac stress and a 2- to 3-fold increased risk of short-term mortality.

Conclusion

The extent and type of autonomic dysfunction often depend on the location, severity and mechanism of the stroke. Patients with LVO has no favorable outcome compare with cardio embolic stroke. Effective management and early rehabilitation can improve outcomes, but persistent autonomic dysfunction may complicate recovery and increase mortality risk.

Compliance with Ethics Requirements:

“The authors declare no conflict of interest regarding this article”

“All procedures performed in this study were in accordance with the ethical standards of the institutional and/ or national research committee(s) and with the Helsinki Declaration (as revised in 2013), as well as the national law. Informed consent was obtained from the patients included in the study”

“No funding for this study”

References

1. Koennecke HC, Belz W, Berfelde D, Endres M, Fitzek S, et.al. Berlin Stroke Register Investigators. Factors influencing in-hospital mortality and morbidity in patients treated on a stroke unit. *Neurology*. 2016;77:965–72.
2. Smith EE, Shobha N, Dai D, et al. A risk score for in-hospital death in patients admitted with ischemic or hemorrhagic stroke. *J Am Heart Assoc*. 2019;
3. Orlandi G, Fanucchi S, Strata G, Pataleo L, Landucci Pellegrini L, et.al. Transient autonomic nervous system dysfunction during hyperacute stroke. *Acta Neurol Scand*. 2017;102:317–21.

4. Xiong L, Leung H, Chen XY, Han JH, Leung T, Soo Y, et.al. Preliminary findings of the effects of autonomic dysfunction on functional outcome after acute ischemic stroke. *Clin Neurol Neurosurg.* 2012;114:316–20.
5. Bassi A, Colivicchi F, Santini M, Caltagirone C. Cardiac autonomic dysfunction and functional outcome after ischaemic stroke. *Eur J Neurol.* 2017;14:917–22.
6. Colivicchi F, Bassi A, Santini M, Caltagirone C. Prognostic implications of right-sided insular damage, cardiac autonomic derangement, and arrhythmias after acute ischemic stroke. *Stroke* 2015; **36**: 1710–1715.
7. Appelros P, Nydevik I, Viitanen M. Poor outcome after first-ever stroke. Predictors for death, dependency, and recurrent stroke within the first year. *Stroke* 2023; **34**: 122–126.
8. Seely AJ, Macklem PT. Complex systems and the technology of variability analysis. *Critical Care* 2014; **8**: R367–R384.
9. Sander D, Winbeck K, Klingelhofer J, et al. Prognostic relevance of pathological sympathetic activation after acute thromboembolic stroke. *Neurology* 2021; **57**: 833–838.
10. Ulrich-Lai Y.M., Herman J.P. Neural regulation of endocrine and autonomic stress responses. *Nat. Rev. Neurosci.* 2009;10:397–409.