# Posterior circulation lesions are more frequently associated with early seizures after a stroke

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## ABSTRACT

Early seizures (ES) following stroke are prevalent among the elderly population, representing the most common type of acquired seizures. This study aimed to determine the incidence of ES and investigate potential associations with various clinical and radiological factors. 260 stroke patients (mean age 72±13.2, 48.5% females) were prospectively enrolled and followed. Baseline demographic data, clinical data, stroke subtype, ES occurrence, National Institutes of Health Stroke Scale (NIHSS) scores, and Alberta Stroke Program Early CT Score (ASPECT) were collected and analyzed. ES was observed in 11.6% of patients with ischemic stroke compared to 7.1% among patients with hemorrhagic stroke. ES occurred more frequently in those with posterior circulation stroke (18.5% *vs.* 7.1%, P=0.008) and those with NIHSS >15 (19.4% *vs.* 8.4%, P=0.04). In a logistic regression analysis that adjusted for vascular risk factors and NIHSS, posterior circulation stroke remained significantly associated with ES, with an odds ratio of 3.14 (95% CI 1.20 to 7.73, P=0.012). This study revealed that ES following stroke is more common in patients with posterior circulation lesions. These findings emphasize the need for further investigation into additional factors that may influence ES occurrence and its impact on stroke management and patient outcomes.

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## Introduction

Stroke is the third leading cause of death and a very important cause of disability.[1] In adults, stroke is an important cause of epileptic seizures and epilepsy.[2,3] Among adults, stroke accounts for approximately 20% of epilepsy cases, making it the primary cause of seizures and epilepsies in this population. In the elderly, complex partial seizures without secondary generalization are the most prevalent form (47.1%), while temporal lobe epilepsy stands as the most commonly diagnosed epileptic disorder (71.4%).[2] Specific auras such as epigastric sensations or *déjà vu* phenomena are less common, and postictal confusion tends to persist longer, with typical symptoms like automatisms occurring rarely. Epileptic seizures are usually more frequent in patients with hemorrhagic strokes, yet due to the higher incidence, ischemic strokes are very important factors in the presentation of seizures.[4,5] Seizures after stroke are classified as either early onset or late onset based on their timing after the brain infarction. The presence of early seizures (ES) after stroke serves as an important prognostic factor, typically associated with an unfavorable outcome characterized by in-

creased mortality rates, prolonged hospital stays, and heightened disability rates.[6]

Several pathophysiological mechanisms have been proposed to explain the occurrence of seizures after stroke, including ion channel dysfunction, neurotransmitter imbalances, elevated cortisol levels in serum, and hemosiderin deposition. Ischemia and hypoxia-induced dysfunction of ion channels weaken the stability of neuronal membranes, leading to metabolic disorganization within the nerve cells.[7] Acute brain injury impairs the sodium ionic pump, causing an influx of sodium into the nerve cells, depolarization, activation of calcium channels, and an increase in intracellular calcium concentration, ultimately resulting in hyperexcitation of neurons and progressive damage to local inhibitory cells. Several risk factors have been identified for the development of stroke-related epileptic seizures, including hemorrhagic stroke, alcohol use, cortical ischemia, hypotension, and stroke severity.[4,7] Furthermore, the etiology of stroke holds prognostic significance, with stroke of cardiac origin showing a greater propensity for seizure occurrence compared to atherosclerotic or lacunar etiologies (lipohyalinosis).[8] In addition to clinical characteristics, radiological markers play an important role in identifying patients at risk for early epileptic seizures. Computed tomography (CT) without contrast is the commonly used diagnostic method for stroke patients.[9] The Alberta Stroke Program Early CT Scan (ASPECTS) quantifies the extent of ischemia on CT scans by systematically evaluating ten brain regions (including seven cortical regions) that are vascularized by the anterior circulation. ASPECTS, as an assessment system, exhibits a significant correlation with patient prognosis after stroke.[9] Electroencephalography (EEG) serves as an adjunctive method for diagnosing epileptic seizures. Identifying predictive factors for the occurrence of epileptic seizures in stroke patients holds clinical importance since ES are associated with an unfavorable prognosis in these individuals.[10]

## Materials and Methods

In this prospective study, we enrolled patients who were hospitalized in the Clinic of Neurology with a diagnosis of stroke. We excluded patients with venous sinus thrombosis, subarachnoid hemorrhage, subdural hemorrhage, epidural hemorrhage, and those with a history of prior epilepsy. The patients were divided into two groups: those who experienced ES after stroke and those who did not. ES were defined as any seizure, whether focal or generalized, that occurred within one week of the onset of stroke symptoms. The diagnosis was made based on clinical observation and electroencephalographic data. We evaluated various demographic, clinical, and radiological factors to determine their role in the occurrence of ES. The study was conducted at the University Clinical Center of Kosovo, which is the only tertiary healthcare center in Kosovo where most ischemic stroke patients are hospitalized and treated at the Clinic of Neurology. We collected data from stroke patients admitted in our clinic between January 1, 2023, and June 30, 2023.

The index date was defined as the date of symptom onset. During this period, we monitored blood pressure in all hospitalized patients and quantified brain lesions on CT scans using the ASPECT method. Additionally, electrocardiogram and carotid ultrasound or supra-aortic CT angiography were performed to determine the stroke etiology. We also assessed lipid levels, urea, creatinine in the blood, temperature, and the severity of stroke using the National Institutes of Health Stroke Scale (NIHSS), categorized into three groups: 0-4, 5-15, and >15. The diagnosis of ischemic stroke was established based on clinical evaluation of neurological changes, radiological images (CT, magnetic resonance imaging, MRI), and observation of the patient by the medical staff. Brain lesions were categorized as either anterior or posterior circulation based on their appearance on CT or MRI. All clinical data of the patients were prospectively collected at the Clinic of Neurology. Stroke etiology was classified as cardiac emboli, strokes caused by large arteries, lacunar, and cryptogenic, based on the underlying cause. Statistical analysis was performed using the SPSS 21 program. We compared the frequency of epileptic attacks between ischemic and hemorrhagic strokes using the chi-square test. Categorical variables derived from assessment systems such as NIHSS and ASPECT were also analyzed using the chi-square test. Continuous variables were compared using the student t-test. Logistic regression models were employed to evaluate different prediction models. We analyzed the correlation of these parameters with the occurrence of early seizures following a cerebrovascular event.

## Results

### Patients clinical and demographical data

This study included a total of 260 patients with stroke, 48.5% of them were females. The average age of the patients was 72.6±13.2 years. Out of the total, 232 patients (89.2%) had ischemic stroke, while 28 patients (10.8%) had hemorrhagic stroke. Among all patients, 29 (11.2%) experienced ES (early seizures), with 27 (11.6%) occurring in patients with ischemic stroke and 2 (7.1%) in patients with hemorrhagic stroke. The mean age of patients who experienced ES was 60.5±13.8 years, as shown in Table 1. In terms of the NIHSS scores, 50 patients (19.2%) had scores less than 5, 131 patients (50.4%) had scores between 5 and 15, and 79 patients (30.4%) had scores greater than 15. The mean value of the ASPECT score was 7.7±1.6.

### Early seizure after ischemic stroke

ES after ischemic stroke was found to be more common in patients who experienced posterior circulation strokes, with a prevalence of 18.5% compared to 7.1% in those without posterior circulation strokes (P=0.008) (Figure 1). Additionally, patients with higher NIHSS (>15) had a higher occurrence of ES after stroke (19.4%), whereas patients with NIHSS <5 (8.3%) and scores between 5 and 15 (8.5%) had lower occurrences. Mean ASPECT scores were lower among patients with ES after stroke (5.78 *vs*. 7.24), P=0.02 (Figure 2).

The presence of vascular risk factors did not show significant differences between the groups. Similarly, there were no notable differences in mean arterial blood pressure and glycemia on admission between patients with and without ES after stroke (Table 2). After adjusting for age, gender, hypertension, diabetes mellitus, smoking, and NIHSS scores

in a logistic regression analysis, it was found that posterior circulation stroke remained significantly associated with an increased risk of ES after stroke, with an odds ratio of 3.14 (95% CI 1.20 to 7.73, P=0.012).

## Discussion

The present study aimed to evaluate the predictors of ES after stroke in a sample of 260 patients with stroke. Our findings suggest that posterior circulation ischemic stroke, lower ASPECT score, and higher NIHSS were all significantly associated with an increased risk of ES after stroke.

There is evidence to suggest that ES after stroke can have a negative impact on patients' outcomes.[5] A study by Šmigelskytė *et al.*[6] also reported that ES after stroke were associated with worse functional outcomes at three months after stroke onset, as well as an increased risk of developing post-stroke epilepsy. The authors suggested that this may be due to the fact that early seizures may exacerbate ischemic brain injury and contribute to the development of post-stroke epilepsy. Therefore, identifying patients at risk of developing ES after stroke and time management of ES in patients with stroke is important in order to improve outcomes and reduce the risk of post-stroke epilepsy.

Our finding that higher NIHSS was associated with an increased risk of early seizures after stroke is consistent with previous studies.[11,12] NIHSS is a widely used measure of stroke severity, and has been shown to be a strong predictor of both short- and long-term outcomes after stroke.[13] The association between stroke severity and seizures may be due to the fact that more severe strokes are associated with greater disruption of inhibitory pathways and a higher risk of cortical spreading depolarizations, which can trigger seizures.[14] However, in a recent meta-analysis including 18 casecontrol studies there were no associations between NIHSS and ES after stroke.[15] The evidence regarding the association between ASPECT score and early seizures after stroke was consistent. Anadani *et al.*[16] found that a lower ASPECTS score <6, was associated with an increased risk of early seizures after ischemic stroke. The authors suggested that this may be due to a greater degree of ischemic injury and disruption of cortical function in patients with lower ASPECTS scores. Another study by Chen *et al.*[9] reported that lower values of ASPECT score and cortical lesions are associated with an increased risk of ES after stroke.

The association between posterior circulation stroke and early seizures after stroke has been previously reported in only one recent study.[17] One possible explanation for this association is that posterior circulation stroke may result in more extensive brain damage and disruption of inhibitory pathways, making patients more susceptible to seizures. It is also possible that the location of the stroke itself may con-

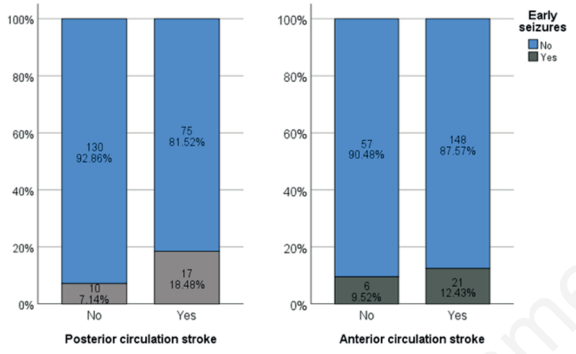


**Figure 1.** Early seizure after ischemic stroke were significantly more frequent in patients with posterior circulation stroke.

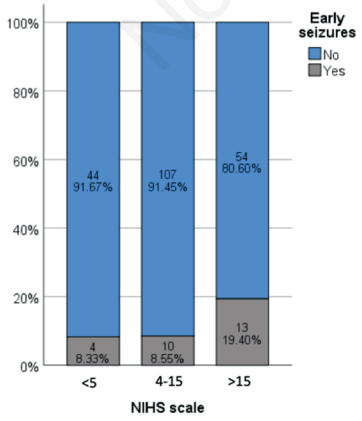


**Figure 2.** Patients with National Institutes of Health Stroke Scale higher than 11 were more frequently associated with ES after stroke compared to patients with National Institutes of Health Stroke Scale <5 and National Institutes of Health Stroke Scale 5-15.

**Table 1.** Patients' clinical and demographical data.

| Variables | n=260 |
|---|---|
| Age (years), mean (SD) | 72 (13.2) |
| Gender (females), n (%) | 126 (48.5) |
| Early seizures, n (%) | 29 (11.2) |
| Lesion location | |
| Anterior circulation | 192 (73.8) |
| Posterior circulation | 98 (37.7) |
| Cortical lesions, n (%) | 84 (32.3) |
| Hypertension, n (%) | 193 (74.2) |
| Diabetes mellitus, n (%) | 93 (35.8) |
| Pre-stroke therapy, n (%) | |
| Antiplatelet | 88 (33.8) |
| Anticoagulants | 13 (5.0) |
| Statins | 41 (15.8) |
| Glucose (mmol/L), mean (SD) | 8.8 (4.7) |
| Cholesterol (mmol/L), mean (SD) | 4.7 (1.3) |
| NIHSS, n (%) | |
| 0-5 | 50 (19.2) |
| 5-15 | 131 (50.4) |
| >15 | 79 (30.4) |
| ASPECT score, mean (SD) | 7.7 (1.6) |
| Stroke type, n (%) | |
| Ischemic | 232 (89.2) |
| Hemorrhagic | 28 (10.8) |

SD, standard deviation; NIHSS, National Institutes of Health Stroke Scale; ASPECT, Alberta Stroke Program Early CT Score.

tribute to the risk of seizures, as the posterior circulation supplies key regions involved in the regulation of cortical excitability.

The posterior brain circulation supplies blood to brainstem, cerebellum, and occipital lobes and some important structures involved in seizure generation and propagation, including the thalamus, hippocampus, and hypothalamus (Figure 3). Disruption of blood flow to these regions due to stroke can lead to altered excitability and connectivity, which may increase the risk of seizures. Early focal seizures following stroke may not always be recognized or reported, particularly if they have aphasia, whereas generalized seizures are more likely to be observed and reported by medical staff or family members.[18] It is possible that the higher frequency of generalized seizures in patients with posterior circulation stroke is related to the fact that hypothalamic lesions, which are commonly associated with posterior circulation stroke, can give rise to various seizure types including secondary generalized seizures, as reported in prior studies.[19] It is possible that temporal lobe ischemia could contribute to the frequency of ES after posterior circulation stroke. The temporal lobe is an important region for seizure generation and propagation, and ischemia in this area could lead to altered excitability and connectivity, potentially increasing the risk of seizures.[19] However, it is important to note that the relationship between temporal lobe ischemia and early seizures after posterior circulation stroke has not been extensively studied and further research is needed to better understand the potential impact of this factor.[20]

Current clinical guidelines typically do not recommend the routine use of anticonvulsive medications as a preventive measure against seizures in patients with acute stroke. However, there is substantial evidence indicating that seizures occurring after a stroke are linked to complications and worst outcome in patients treated with thrombolysis and thrombectomy.[16,21] Consequently, it may be advantageous to consider treatment with anticonvulsive medications for a specific subset of patients at increased risk of experiencing ES after stroke. In addition to anticonvulsive therapy,[22] it was recently reported in a meta-analysis that statin therapy is associated with decreased risk of ES after stroke.[23]

## Study limitations

There are several limitations to our study that should be considered when interpreting the results. First, brain imaging was limited to CT scans and did not include MRI. MRI is known to be more sensitive in detecting subtle brain changes and may have identified additional factors associated with ES after stroke. Second, EEG monitoring was not performed in our study, which may have resulted in underreporting of subclinical seizures. Third, seizures were mainly reported



**Table 2.** Comparison of different variables between patients with and without early seizures after ischemic stroke.

| Variables | ES after ischemic stroke | | P-value |
|---|---|---|---|
| | Yes | No | |
| Age, years | 71.8 (12.8) | 72.1 (13.2) | 0.89 |
| Gender | | | |
| Females | 11 (9.7) | 102 (90.3) | 0.37 |
| Males | 16 (13.4) | 103 (86.6) | |
| Smoking | | | |
| Yes | 22 (11.6) | 168 (88.4) | 0.95 |
| No | 5 (11.9) | 37 (88.1) | |
| Hypertension | | | |
| Yes | 19 (13.1) | 126 (86.9) | 0.23 |
| No | 8 (9.1) | 79 (90.9) | |
| Diabetes mellitus | | | |
| Yes | 7 (8.0) | 80 (92.0) | 0.18 |
| No | 20 (13.8) | 125 (86.2) | |
| Atrial fibrillation | | | |
| Yes | 8 (18.2) | 36 (81.8) | 0.13 |
| No | 19 (10.1) | 169 (89.9) | |
| Anterior circulation stroke | | | |
| Yes | 21 (12.4) | 148 (87.6) | 0.54 |
| No | 6 (9.5) | 57 (90.5) | |
| Posterior circulation stroke | | | |
| Yes | 17 (18.5) | 75 (81.5) | 0.008 |
| No | 10 (7.1) | 130 (92.9) | |
| NIHSS | | | |
| <5 | 4 (8.3) | 44 (91.7) | 0.04 |
| 5-15 | 10 (8.5) | 107 (91.5) | |
| >15 | 13 (19.4) | 54 (80.6) | |
| ASPECT | 5.78 (2.1) | 7.24 (2.3) | 0.02 |
| Mean arterial pressure on admission | 102 (21) | 104 (19) | 0.53 |
| Glycaemia on admission | 8.6 (6.5) | 8.9 (4.6) | 0.84 |

ES, early seizure; NIHSS, National Institutes of Health Stroke Scale; ASPECT, Alberta Stroke Program Early CT Score.

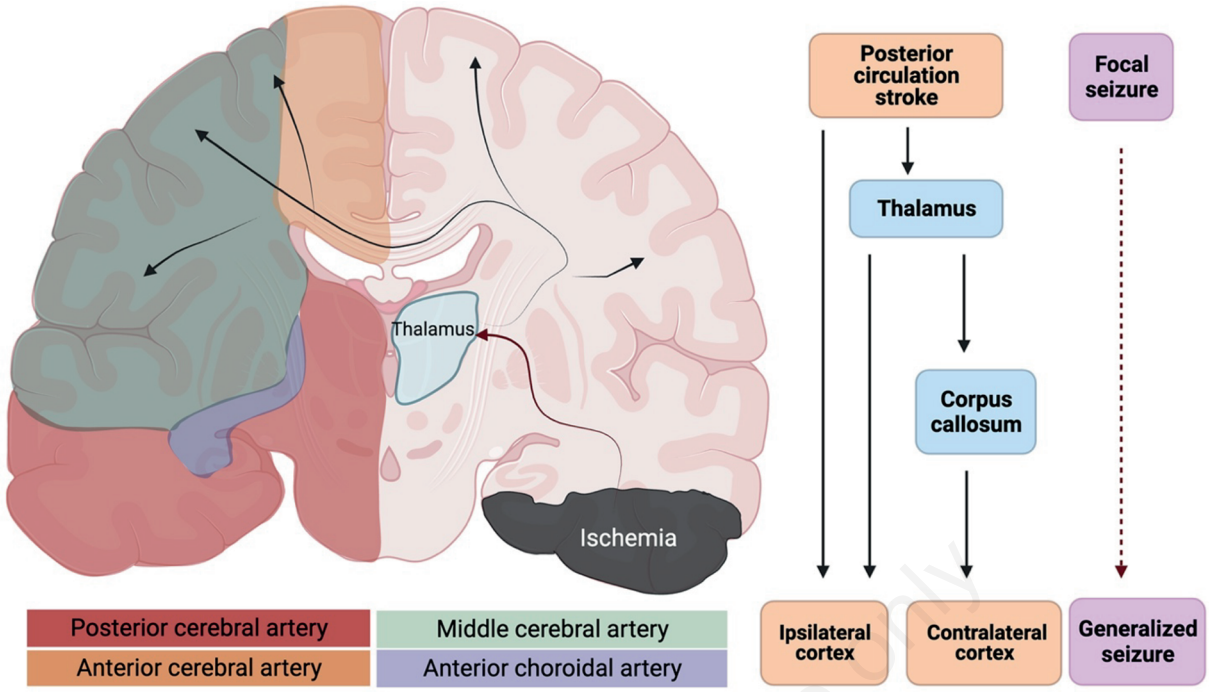


**Figure 3.** Brain vascularization and routes of depolarization spread and generalization of posterior circulation derived focal seizures. Posterior cerebral artery supplies blood in the brain territories that are involved in both seizure generation and propagation.

by patients and family members, which may have led to underestimation of the true incidence of seizures. Fourth, the short follow-up time in our study did not allow us to identify stroke etiology for most patients, which may have influenced our findings. Finally, our study was conducted at a single center, which may limit the generalizability of our results to other settings.

## Conclusions

In this study, it was observed that seizures occurring after ischemic stroke were more prevalent among patients with posterior circulation stroke, as well as among those with larger infarctions and higher levels of neurological deficits. Currently, there is no approved treatment for preventing seizures in stroke patients. Nevertheless, focusing on a specific subset of patients who would potentially benefit from preventive medication could lead to improved outcomes, particularly following intervention procedures like thrombolysis or thrombectomy. These findings underscore the importance of conducting further research to identify additional factors that could affect the occurrence of post-stroke seizures and their implications for stroke management and patient outcomes.

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