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Predictors and Outcome of Early Post Stroke Seizures

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ABSTRACT

Background: In adults, stroke is the leading cause of epilepsy. Seizures that occur after a stroke are of two distinct types; those that manifest early after the stroke and those that manifest much later the clinical course and occurrence of late seizures can be considerably influenced by early seizures. The objective of the current study is to investigate the predictors of early seizure after an acute ischemic stroke and the impact of these seizures on outcome of the patients.

Patients and methods: A case-control study was conducted in the intensive care unit (ICU) of Neurology Department, Zagazig University Hospitals and New Mansoura General Hospital. A total of 60 subjects were included: 30 patients with acute ischemic stroke with early seizures (case group) and 30 patients with acute ischemic stroke without seizures (control group). Evaluation of the severity of neurologic deficits was done by using National Institutes of Health Stroke Scale (NIHSS). All patients' short-term outcomes were evaluated using a modified Rankin Scale.

Results: There was a statistically significant higher mean NIHSS score and mean Modified Rankin scale among the case group than the control group. The etiologies of ischemic stroke were 46.7% of the cases had cardio embolic stroke, 40% atherosclerotic and 13.3% lacunar. The distribution of the ischemic stroke according to infarction size was 56.7% large, 30% medium and 13.3% small. Among the case group 53.3% had cortical involvement and 30% had hemorrhagic transformation. **Conclusion:** Predictors of early post-acute ischemic stroke seizures were large infarction size, cortical site, and patients with hemorrhagic transformation. Also, early post-acute ischemic stroke seizures were associated with more severe disease and poor outcome.

Keywords: Post Ischemic Stroke, Early Seizures, Late Seizures, National Institutes of Health Stroke Scale, Modified Rankin scale.

INTRODUCTION

Ischemic or hemorrhagic focal alteration of cerebral blood flow causes abrupt neurologic dysfunction, or stroke. Stroke can result in permanent brain impairment, incapacity, or death depending on the severity of the cerebrovascular abnormality [1].

One of the most prevalent causes of epilepsy in adults is cerebrovascular illness. Cardioembolic infarction and cortical anomalies are frequently linked to post-stroke seizures. Between 39% and 45% of all elderly seizures occur after a stroke and can be further subdivided into early and late stages based on the two-week post-stroke interval that is typically used to define the onset of seizures following a stroke [2]. Seizures are classified as either early (those occurring within the first week or two after a stroke) or late (those occurring more than two weeks after the stroke)[3].

The aim of this study was the prediction of patients who will have an early seizure after an acute ischemic stroke and the impact of these seizures on outcome of the patients.

PATIENTS AND METHODS

The present study was a case-control study conducted in the intensive care unit (ICU) of Neurology Department, Zagazig University Hospitals and New Mansoura General Hospital, during the period from October 2020 to October 2021.

Patients with acute ischemic stroke with ages≥ 18 years who had seizures within one week from the onset of stroke and patients with Computed tomography (CT) and /or Magnetic resonance imaging (MRI) evidence of an acute ischemic stroke and no other possible explanations of their neurologic impairments (such as a tumor, trauma, infection, or vasculitis). Patients having a known history of epilepsy and those who had suffered a stroke, subarachnoid hemorrhage, or cerebral venous thrombosis were not included in the study.

All patients were subjected to history taking and proper general and neurological examination. The National Institutes of Health Stroke Scale (NIHSS) was used to assess the extent of neurological impairment [4]. All patients' short-term outcomes were evaluated using a modified Rankin scale [5].

Ethical consent:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University (IRB approval # (6411-30-09-2020), and an enlightened written consent was taken from every patient in this study. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical analysis

The collected data were coded, processed and analyzed using the Statistical Package for Social Sciences (SPSS) version 20 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean and standard deviation (SD). Independent samples t-test was used to compare between two independent groups

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of normally distributed variables (parametric data). P value ≤0.05 was considered significant.

RESULTS

The average ages of patients and controls do not differ significantly from one another (**Table 1**).

Table (1): Comparison of age between patients and control groups.

Variable	Age (mean ± SD)	Student t test
Patients group	50.25 ± 4.25	t=0.818
Control group	51.08 ± 3.58	p=0.417

Statistically significant higher mean NIHSS score among cases than control group (**Table 2**).

Table (2): Comparison of NIHSS score between patients and control groups

Variable	NIHSS (mean ± SD)	Student t test
Patients group	27.47 ± 3.97	t=4.82
Control group	21.27 ± 5.81	p<0.001*

There was statistically significant higher mean Modified Rankin scale among cases than control group (**Table 3**).

Table (3): Comparison of Modified Rankin scale between patients and control groups

Variable	Modified Rankin scale score (mean ± SD)	Student t test
Patient group	2.96 ± 1.13	t=2.68
Control group	2.13 ± 1.03	p=0.01*

Table 4 summarizes ischemic stroke etiology and size of infract. Among studied cases; 53.3% have cortical involvement and 30% hemorrhagic transformation (**Table 4**).

Table (4): Frequency of early seizures according to stroke characteristics

Variable	Cases group (n=30)	
Ischemic stroke etiology	**n**	**%**
- Cardio embolic	14	**46.7**
- Atherosclerotic	12	**40.0**
- Lacunar	4	**13.3**
Size of infarct:		
- Small	4	13.3
- Medium	9	30.0
- Large	17	56.7
Cortical involvement	16	53.3
Hemorrhagic transformation	9	30.0

DISCUSSION

Research indicates that between 5 and 20% of patients with stroke get PSS. Two distinct categories exist for these conditions: early onset (ES) and late onset (LS). The dividing line is arbitrary, however seizures that start within a week of a stroke are typically classified as LS [6].

This distinction is significant since the underlying seizure inducing mechanisms and the risk of progression to epilepsy are diverse between the two conditions. Acute neuronal damage, together with glutamate-mediated excitotoxicity, a compromised blood-brain barrier, and ion channel dysfunction, all contribute to the development of ES [7].

The functional outcome and death rate of stroke survivors are negatively impacted by post-stroke symptoms (PSS). Experiments on animals have shown that repeated ES might increase infarct size and hinder recovery. This may occur because of the elevated metabolic needs of the penumbral tissue close to the ischemia zone, which are brought on by the seizure [8].

Our study was set out to examine the factors that lead to seizures developing quickly after an ischemic stroke begins, as well as the effect these seizures on the patients' short-term prognosis.

Thirty patients with acute ischemic stroke who experienced seizures within a week of stroke onset were compared to thirty patients with acute ischemic stroke who did not have seizures.

The present study revealed that the mean age of cases was 50.25 (SD 4.25) years. Reduced cortical excitability with age may explain why patients with early-onset seizures tend to be younger in age [9]. Similarly, **Feyissa *et al.*** [10] revealed that the prevalence of stroke-related epilepsy increased from 1.6% to 10.7% between the ages of 65 and 85 (P <0.001). Also, **Castro-Apolo *et al.*** [10], found that PSS were shown to be substantially higher in patients younger than 65 compared to those older than 85.

No statistically significant variation in risk factor distribution was observed across groups in the current investigation. The highly frequent of risk factor was hypertension and least frequent was obesity (p >0.05).

This is in contrary with the results of **Agarwal *et al.*** [12] who discovered that all risk factors for stroke were evenly distributed between the two groups except hypertension, which was shown to be prevalent in those with ES at a much lower frequency, and the results of **Lahti *et al.*** [13], who found that the prevalence of PSSs was lower in hypertensive patients, despite the fact that the exact pathophysiology was not determined; these authors also noted that the ischemic penumbra is electrically irritable and could serve as the focal point for seizure activity. Maintaining its perfusion with increased blood pressure may prevent seizure activity.

Thrombolysis was not shown to be linked to the development of PSS in the risk factors analysis. This may be the case since thrombolytics have been shown to reduce infarct volume, so guarding against PSS, and their putative neurotoxicity may counteract any potential epileptogenicity [13]. Conversely, anticoagulant use was also found to be linked to an increased risk of ES. Possible causes include the irritating and predisposed nature of hemorrhagic

transformation tendencies associated with their use [14-15].

Fifty-three percent of the PSS cases examined here had cortical involvement. Previous research indicated that infarcts in the cortex, especially those in the middle cerebral artery area, increase the probability of PSS returning [16]. This is consistent with the findings of **Castro-Apolo *et al.*** [11], who found that individuals with PSS had a greater rate of infarcts in the anterior circulation.

Agarwal *et al.* [12] reported that infarct site was a major determinant of whether or not early seizures occurred, with cortical location predisposing to the PSS. Cortical involvement is the most important risk factor for the development of PSS, as demonstrated in **Misirli *et al.*** [17] study. The corresponding OR was 4.25. PSS was also linked to the subtype of stroke caused by major artery disease. This may be due to the fact that infarct volumes and cortical brain tissue involvement are greater in patients with major artery disease, making PSS more likely.

In the present study according to infarction size in studied cases with PSS; 56.7% were large, 30% were medium and 13.3% were small. Similarly, Repeated ES has been linked to larger infarcts and slower recoveries in the past. The higher metabolic demands of the penumbral tissue close to the ischemia zone may cause this [18].

To better understand and treat PSS, several studies have shown risk factors for its occurrence. For example, in a prospective community-based study with a cohort of 1197 patients with stroke over a period of 7 years, 38 individuals (3.2% of the total) developed PSS. Increased rates were seen with older age, intracerebral hemorrhage, larger lesions, and more severe strokes, as well as in cases where preexisting seizure disorders were present [19]. Similarly, a prospective analysis of 1897 patients conducted over 9 months found that the risk of seizures due to hemorrhagic stroke was approximately twice that of ischemic stroke [20]. Patients who suffered a hemorrhagic stroke were excluded from our study in favor of those who had an ischemic stroke.

In the present study, there was a statistically significant higher mean NIHSS score among the patient group than the control group (27.47 versus 21.27) ($p < 0.001$). Also, there was statistically significant higher mean Modified Rankin scale score among the patient group than the control group (2.96 versus 2.13) ($p = 0.01$).

This is consistent with the findings of **Agarwal *et al.*** [12], who found that patients who experienced an early seizure had a significantly worse functional outcome at 3 months after their initial episode of stroke, and with the findings of **Tanaka and Ihara** [2], who found that A higher NIHSS Stroke Scale score indicates a greater degree of early neurologic impairments and disability after a subsequent PSS.

However in contrary to our results **Castro-Apolo *et al.*** [11] found that Stroke severity was not found to be a significant predictor of PSS when the NIHSS Stroke Scale was taken into account ($p=0.21$).

Thirty percent of the patients in this study who were diagnosed with PSS went on to develop hemorrhagic transformation. Multiple case series that looked at the PSS's effect on stroke outcomes found a significant link between PSS and both the short-term and long-term result ($p < 0.001$ and < 0.001, respectively) [11,21]. These results are in line with those of a major retrospective study undertaken by researchers at the Mayo Clinic, which indicated that patients who suffered their first seizure after their first ischemic stroke had a worse functional outcome as measured by the mRs ($p < 0.005$) [22].

Castro-Apolo *et al.* [11] found that PSS patients had a greater risk of overall morbidity and death, were younger, and more frequently experienced severe strokes and ICU admissions ($p < 0.05$). There has been research linking PSS to increased risk of death, longer hospital stays, and more severe impairment. Clinicians should be aware of the poorer prognosis seen in PSS patients so that they can give effective care and family counseling.

On average, people with epilepsy have a higher mortality rate than the overall population. Patients with PSS have a higher risk of dying from their seizures since they occur alongside diffuse vascular dysfunction. Unfortunately, we still don't know how much of a role epilepsy has in the high mortality rate seen in these patients [23].

The overall mortality rate for stroke survivors was 3.56 times the national average in a large cohort of 7740 patients. In 14% of the cases, the cause of death was determined to be repeated seizures. In this cohort, vascular problems were the leading cause of death, but the effect of PSS on mortality was considered clinically significant [24].

According to **Castro-Apolo *et al.*** [11], the most common semiology is a focal to widespread convulsive seizure. Convulsive seizures are a known risk factor for sudden unexpected death in epilepsy, which may explain why stroke patients have a higher mortality rate. It has not been established in previous studies that patients who were administered recombinant TPA had a higher incidence of PPS.

In conclusion, infarct size, cortical location, and patients with hemorrhagic transformation were predictors of early post-acute ischemic stroke seizures. Also, early post-acute ischemic stroke seizures were associated with more severe disease and poor outcome.

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