Hypertension on admission is associated with a lower risk of early seizures after stroke

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ABSTRACT

Purpose: Despite the common occurrence of early seizures (ES) after stroke, the relationship between risk factors and this complication of stroke is not well established. In this study we have examined the relationship between clinical measures on admission and ES after stroke.
Methods: We included 1073 patients (mean age 69 ± 12, 51.6% females) with ischemic and haemorrhagic stroke. The frequency of seizure occurrence within 2 weeks of stroke was determined. We used a logistic regression model to analyse the effect of blood pressure on admission and other clinical factors (age, gender, diabetes, atrial fibrillation and dyslipidemia) on the occurrence of ES after stroke.
Results: ES occurred after 4.1% and 4.0% of ischemic and haemorrhagic strokes respectively. Compared to patients with high blood pressure on admission, those with low and normal blood pressure had a higher risk of ES after stroke (2.9% vs.7.5% vs. 7.6%, $p = 0.001$). Also the mean age of patients with post-stroke ES was lower (62.5 vs. 69.3, $p < 0.001$). In a logistic regression analysis, low/normal blood pressure remained independently associated with ES after stroke with OR of 2.46 (95% CI 1.38–4.63, $p = 0.006$).
Conclusion: ES after stroke was equally frequent in patients with ischemic and haemorrhagic stroke. Low/normal blood pressure on admission and younger patient age were risk factors for ES after stroke.
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1. Introduction

Stroke registry data shows that approximately 5–20% of all stroke patients will have subsequent seizures, but epilepsy (recurrent seizures) will develop in only a small subset of this group [1,2]. Stroke is the most common cause of seizures among the elderly, accounting for 39–45% of all seizures [3–5]. Seizures can occur either during the acute phase of the stroke or during the following months. According to their timing after brain ischemia, seizures after stroke are classified as early or late onset. The most accepted cut-off point to distinguish between the two is 2 weeks after the presenting symptoms [2,6].

The prevalence of seizure after stroke and its pathophysiological mechanism differ between stroke subtypes. It was shown that the prevalence of subtypes of early seizure (ES) after stroke vary between 1.8% and 6.2% for ischemic stroke [7,8], 2.8–18.7% for intracerebral haemorrhage (ICH) [7,9], and 2.7–16.4% for subarachnoid haemorrhage (SAH) [10]. In the Seizure After Stroke study [11], 42% of all patients who experienced seizure had the first attack within 24 h of the stroke; furthermore, most seizures associated with haemorrhagic stroke occurred at the onset or within the first 24 h. During acute ischemic injury, the accumulation of intracellular calcium and sodium may result in depolarization of the transmembrane potential and other calcium-mediated effects [12–14].

Among the generally accepted risk factors associated with ES after stroke are the level of the patient's disability, age, volume of infarction/haemorrhage and hyperglycaemia [10]. In the present study, we evaluated the frequency of ES after stroke in different stroke subtypes and its association with the clinical characteristics of patients on admission as well as their risk factors. We also aimed to evaluate the previously reported data suggesting that ischemic strokes caused by cardiac embolization are more frequently associated with ES after stroke than stroke of other aetiologies [15,16].

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2. Methods

2.1. Inclusion and exclusion criteria

The University Clinical Centre of Kosovo (UCCK) is the only tertiary health care centre in Kosovo. Most acute stroke patients in Kosovo are admitted to the Neurology Clinic, UCCK.

We retrospectively analysed data of all of the patients admitted to the hospital from January 1, 2013 to December 31, 2013. In total, 1073 patients (mean age 69 ± 12, 51.6% females) with ischemic or haemorrhagic stroke were included in this study. Patients with a history of epilepsy were excluded from the study. In patients with venous sinus thrombosis, we only evaluated the frequency of ES after stroke, but they were not included in subgroup analysis because it was reported to be a highly epileptogenic condition [5].

2.2. Definitions and clinical data collection

The diagnosis of stroke was based on direct observation by the medical staff during admission or the hospitalization period, clinical signs and imaging (computed tomography (CT) and magnetic resonance imaging (MRI)) results. The diagnosis of seizures after stroke in addition to in-hospital observation was based on descriptions obtained from the ambulance crews or patients' family members. All of the patients included in this study underwent a neurological re-evaluation provided by a neurologist on an outpatient basis within a 2–4 week period after discharge. When early seizures after stroke occurred after the patients' discharge from the hospital, the information provided after their re-hospitalization or during outpatient evaluation were collected and recorded in their history.

Blood pressure (BP) on admission was considered to be the average of all readings (median = 2) obtained in the emergency department and admission room before the administration of any antihypertensive drugs. All patients underwent a CT scan within 24 h after admission and a second one within 72 h when necessary. An electroencephalogram was performed on every patient suspected of having a seizure. All patients with ischemic stroke were investigated with carotid Doppler and ECG; most also received transthoracic echocardiography. Prognostic risk factors were assessed for each patient, including age, gender, serum glucose, hypertension (defined as the use of antihypertensive agents, a systolic blood pressure >140 mm Hg or a diastolic blood pressure >90 mm Hg), prior stroke, prior/on-going coronary artery disease, atrial fibrillation, diabetes mellitus, hypercholesterolemia (defined as the use of antihyperlipidaemic agents or a serum cholesterol level >220 mg/dl), current smoking (defined as a history of smoking during the preceding 3 months). In addition, information about the patient's medication at stroke onset was determined. The morning after admission, fasting blood samples were taken to determine complete blood count (CBC), cholesterol concentration, serum glucose level, and liver and kidney function tests.

According to the time to seizure occurrence after stroke onset, seizures were defined as early onset if they occurred within 2 weeks and late onset if they occurred after 2 weeks. In this study, we included and analysed only seizures that occurred within the first 2 weeks after initial symptoms.

2.3. Statistical analyses

Categorical variables were expressed as percentages and continuous variables were expressed as the means $\pm$ standard deviations (SD). We used Student's t-test to compare the mean age (continuous variable) between patients with and without ES after stroke, and for the remaining comparisons, we used the chi-square test with a pre-selected significance level of $p < 0.05$. Logistic regression models were used to determine the relationship between ES after stroke and stroke subtypes and between ES after stroke and clinical data on admission and other risk factors. All statistical analyses were performed using IBM SPSS Statistics 22.

3. Results

3.1. Patients' data

We included 1073 patients (mean age 69 ± 12, 51.6% females) in this study; the patients' characteristics are shown in Table 1. Approximately 794 patients had ischemic stroke, 148 patients had haemorrhagic stroke, 121 patients had subarachnoid haemorrhage and 10 patients had venous sinus thrombosis. Stroke recurrence was identified in 66 patients with ischemic stroke, six patients with haemorrhagic stroke and only one patient with subarachnoid haemorrhage. A total of 732 patients presented with hypertension, whereas 292 had normal blood pressure and 39 had low blood pressure.

3.2. Early seizure after different stroke subtypes

The numbers and proportions of patients with ES after stroke according to the sub-group were 4.1% ($n = 33$) in the 794 patients with ischemic stroke, 4.0% ($n = 6$) in the 148 patients with haemorrhagic stroke, 3.8% ($n = 4$) in the 121 patients with subarachnoid haemorrhage and 10% ($n = 1$) in the 10 patients with sinus venous thrombosis.

The occurrence of ES after stroke was higher in patients with recurrent stroke: 9.5% ($n = 7$) of the 73 patients.

3.3. Early seizure after stroke and risk factors

Table 2 shows that patients who presented with lower and normal blood pressure on admission had a higher risk of ES after stroke compared to those who presented with higher blood pressure (7.6% and 7.5% vs. 2.9%, respectively, $p = 0.001$). Furthermore, ES after stroke was higher among patients aged <65 years compared to patients aged ≥65 years (6% vs. 3.3%, $p = 0.042$). The mean age of patients with early seizures after stroke was 62.5 years compared to 69.3 years in patients who did not suffer ES after stroke, $p < 0.001$ (Fig. 1).

Table 3 shows that after logistic regression analysis of potential predictors (blood pressure, age, gender, diabetes, atrial fibrillation and dyslipidaemia) and relevant confounders, low/normal blood pressure remained independently associated with ES after stroke, with an OR of 2.84 (95% CI, 1.57–5.16, $p < 0.001$). Analysis of patients with only ischemic stroke showed that the association between blood pressure and ES after stroke remained significant, with an OR of 2.46 (95% CI, 1.38–4.63, $p = 0.005$).

Table 1
Patients' data.

Age, mean $\pm$ SD	69 ± 12
Gender (females), n (%)	514 (48.4)
Hypertension, n (%)	732 (68.9)
Diabetes mellitus, n (%)	245 (23)
Atrial fibrillation, n (%)	68 (6.4)
Dyslipidemia, n (%)	70 (6.5)
Antiagregation therapy, n (%)	573 (53.9)
Anticoagulation therapy, n (%)	79 (7.4)
Statins, n (%)	182 (17.1)
ACE inhibitors, n (%)	406 (38.2)
Calcium channel blockers, n (%)	58 (5.5)