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Original Article

Clinical analysis on high risk factors for epilepsy after acute stroke

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Abstract: Objective: To explore the risk factors for epileptic seizure after stroke for the purpose of guiding clinical practice. Methods: The clinical data of 358 cases of stroke patients admitted to our hospital from June 2012 to June 2015 were analyzed retrospectively in a case-control study. Stroke patients with confirmed epilepsy were enrolled in the research group and those without epilepsy were included in the control group. Risk factors related to epilepsy after stroke were statistically analyzed and univariate and multivariate Logistic regression analyses were performed. Results: The incidence of epilepsy after stroke was 9.48% (n=31) in 358 patients with stroke. Univariate analysis showed that subtype, site, and range of stroke and neurological severity score (NSS) were significantly associated with epileptic seizure after stroke (P<0.05). Multivariate Logistic regression analysis showed that cardioembolism, cortical lesions, neurological severity score >20 and multi-lobar lesions were risk factors for epileptic seizure after stroke (P<0.05). The incidence of epilepsy after stroke was high in patients with cardioembolism, cortical lesions and high NSSs. Conclusion: Stroke patients with stroke subtypes including cardioembolism, lesions in cortex, and high NSSs are more likely to be attacked by secondary epileptic seizure.

Keywords: Ischemic stroke, hemorrhagic stroke, epileptic seizure, risk factors

Introduction

Cerebral apoplexy (CA) is an acute cerebrovascular disease, also known as "stroke" or "cerebral vascular accident" (CVA). It is a set of diseases of brain tissue circulatory dysfunctions caused by sudden rapture or blockage of blood vessels in the brain. There are ischemic and hemorrhagic strokes [1]. Ischemic stroke, accounting for 60%-70% of stroke patients overall, has a higher incidence than hemorrhagic stroke [2]. This disease can lead to hemiplegia and some other symptoms in patients, greatly impacting their quality of life. It may also cause epilepsy or other complications. Epilepsy after stroke refers to epileptic seizure that occurs at certain time after stroke in patients who have no history of epilepsy before stroke, no cerebral or other metabolic diseases [3]. According to data statistics in the literature, more than 50% newly-diagnosed epilepsies in elderly patients are caused by stroke. Secondary epilepsy after stroke can increase mortality and difficulty in management of strokes. As a result, the life quality of patients with stroke decreases. With the improvement of quality of life, the incidence of stroke is increasing on a yearly basis. It is imminent to know the risk factors for epilepsy after stroke and to improve the efficiency of early clinical prevention and treatment. Therefore, we selected 358 patients and made a retrospective analysis on their clinical data, as reported in the following sections.

Materials and methods

General data

The subjects consisted of 358 patients who were admitted to our hospital form June 2012 to June 2015 for stroke treatment. The patients included 246 males and 112 females, aged from 45 to 75 (mean, 63.7 years, s=10.6). Inclusion criteria: Patients who were diagnosed as having stroke as documented on brain CT or MRI scans and eligible for the diagnostic criteria for stroke approved at The Fourth National Conference on Cerebrovascular Diseases [4].

Table 1. Univariate analysis of epilepsy after stroke

Univariate	Research group (n=31)	Control group (n=327)	χ^2	P
Sex male	21	225	0.015	0.903
Female	10	102		
Age <60	17	181	0.003	0.956
Age ≥60	14	146		
Smoke history	11	115	0.001	0.972
Hypertension				
Level 1	5	62		
Level 2	10	90	1.808	0.179
Level 3	12	153		
Type 2 diabetes mellitus	12	131	0.022	0.883
Hyperlipidemia	18	150	1.690	0.194
Coronary heart disease	15	102	3.805	0.051
Stroke subtype				
Nontrauma cerebral hemorrhage	13	81	4.309	0.038
Subarachnoid hemorrhage	9	65	1.447	0.229
Cerebral infarction	20	136	6.053	0.014
Cardio embolism	25	189	6.147	0.013
Stroke site				
Cortical lesions	20	120	9.202	0.002
Subcortical lesions	11	207		
Range of stroke				
Uni-lobe lesions	13	223	8.692	0.003
Multi-lobar lesions	18	104		
NIHSS score				
<20	9	236	24.394	0.000
≥20	22	91		

Exclusion criteria: (1) Patients with a history of epilepsy before stroke; (2) Those with epilepsy caused by other factors; (3) Those with severe symptoms after stroke associated with severe multiple organ dysfunctions. This trial was approved by the ethics committee on clinical research. All the patients signed written informed consents in a sober state.

Research methods

A total of 358 patients were divided into two groups. According to the above inclusion criteria, patients confirmed with diagnosed as having epilepsy after stroke were enrolled in the research group while the stroke patients without epilepsy were included in the control group. The patients' relevant clinical data were analyzed respectively, including patients' (1) general information like gender, age, personal history, and complications (hypertensive disease, type 2 diabetes mellitus, hyperlipidemia, or coronary heart disease), (2) stroke subtypes: subarachnoid hemorrhage, non-trauma cerebral hemorrhage, cerebral infarction, and cardiogenic brain embolism, (3) lesion sites: cortical stroke and subcortical stroke; (4) range of lesions: uni-lobar stroke, and multi-lobar stroke; (5) National Institute of Health Stroke Scale (NIHSS) score: mild neurologic impairment (NIHSS scores ≤10); moderate neurologic impairment (NIHSS scores, 11-19); and severe neurologic impairment (NIHSS scores ≥20). The above clinical data were analyzed using univariate and multivariate Logistic regressions. Patients with acute stroke were treated with conventional drugs for cerebral infarction, and closely observed. Relevant clinical resuscitative measures were taken based on the severity of attacks and type of early epileptic seizure.

Statistical analyses

Data were analyzed using SPSS statistical software (version 17.0). Univariate analysis was

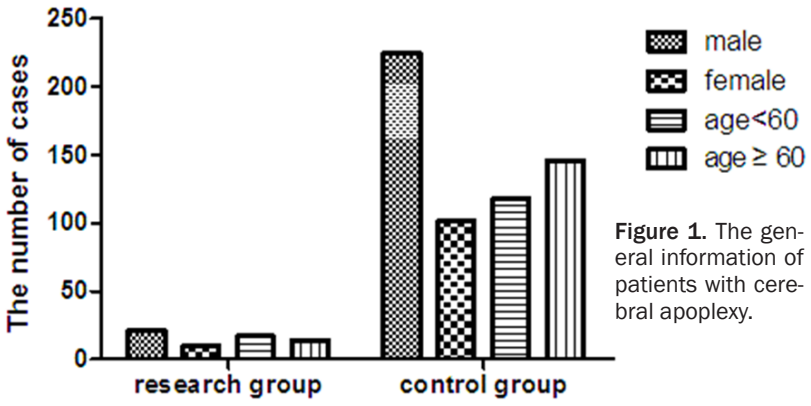

Figure 1. The general information of patients with cerebral apoplexy.

performed using the χ^2 test. Multivariate Logistic regression analysis was used to analyze risk factors for epileptic seizure after stroke. With the significance level (α=0.05), P<0.05 is considered statistically significant.

Results

Univariate analysis

As shown in **Table 1**, compared with the control group, the research group had 4 risk factors (P≤0.05), which were subtype stroke, lesion site, range of lesions, and NIHSS score. But general data, such as gender, age (**Figure 1**), smoke history, complications (hypertension, type 2 diabetes mellitus, coronary heart disease, and hyperlipidemia) showed no significant difference between the research group and the control group (P>0.05).

Stroke subtypes

Cerebral hemorrhage occurred in 13 patients in the research group and 81 in the control group, and the difference was significant (P=0.038). Twenty cases of Cerebral infarction occurred in 20 patients in the research group and 136 in the control group, so the difference was significant (P=0.014). Cardiogenic brain embolism occurred in 25 patients in the research group and 189 in the control group, so the difference was significant (P=0.013). **Table 1** shows cerebral hemorrhage, cerebral infarction, and cardiogenic brain embolism are the major risk factors for epilepsy after stroke.

Lesion sites

Cortical lesions occurred in 20 patients in the research group and 120 in the control group, so the difference was significant (P=0.002). **Table 1** shows cortical lesion is also a major risk factor for epilepsy after stroke.

Range of lesions

Multi-lobar lesions occurred in 18 patients in the research group, and 104 cases in the control group. There was a significant difference between the two groups (P=0.003). **Table 1** shows multi-lobar lesions is also a major risk factor for epilepsy after stroke.

NIHSS

There was a significant difference between NIHSS<20 and NIHSS≥20 (P=0.000), showing that the degree of neurologic impairments, namely, the severity of stroke is also a major risk factor for post-stroke epilepsy (**Figure 2**).

Multivariate analysis

On the univariate analysis, multivariate analysis indexes and quantitative criteria are shown in **Table 2**. Significant independent variables were analyzed using multivariate Logistic regression. It shows that the risk factors independently effecting epileptic seizure after ischemic stroke included cardiogenic cerebral embolism, cortical lesions, NIHSS and multi-lobar lesions.

Discussion

Cerebrovascular diseases are clinically common and frequently-encountered diseases, including cerebral atherosclerosis, thrombosis, stenosis, occlusion, cerebral arterial injury, and cerebral aneurysms [5], with the common feature causing ischemic or hemorrhagic accidents in the brain tissues. Cerebrovascular diseases could greatly affect patients' health and quality of life, resulting in their inability to take care of themselves and a variety of complications including secondary epilepsy which increases mortality and morbidity of the patients [6]. Thus, it is crucial to properly evaluate the risk factors for early-onset epilepsy after cerebral hemorrhage in clinical prevention and treatment.

In our study, we retrospective analyzed the data of stroke patients admitted to our hospi-

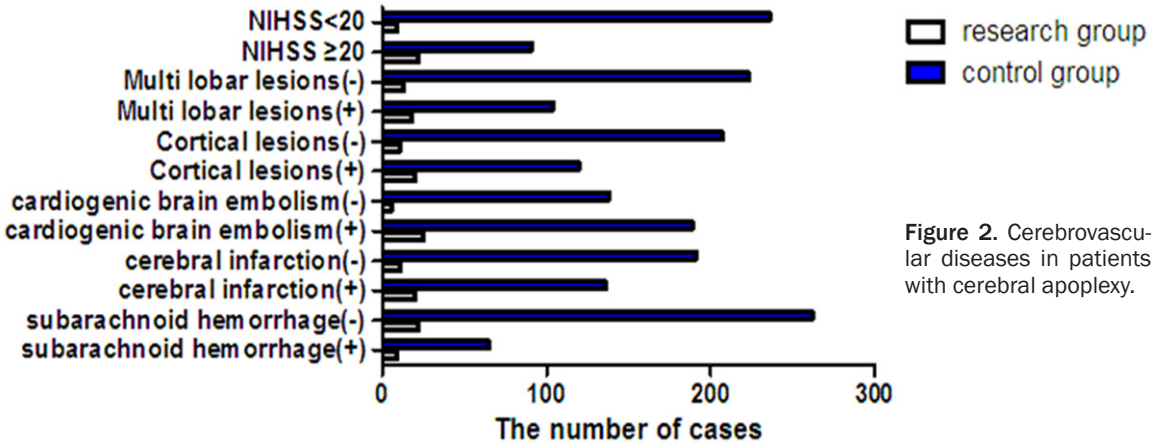

Figure 2. Cerebrovascular diseases in patients with cerebral apoplexy.

Table 2. Multivariate Logistic regression analysis on epilepsy after acute cerebrovascular diseases

Risk factors	Regression coefficient	Wald value	OR value	P	95% CI
Coronary heart disease	0.03	0.005	1.031	0.942	0.451-2.355
Subarachnoid hemorrhage	-7.98	2.708	0.454	0.100	0.177-1.163
Brain infarction	0.236	0.284	1.266	0.594	0.532-3.013
Cardiogenic brain embolism	0.105	5.287	1.111	0.048	1.001-1.232
Cortical lesions	1.747	7.052	2.110	0.000	1.917-2.322
Multi-lobar lesions	2.704	7.613	2.021	0.000	1.716-2.379
NIHSS score	1.722	9.387	5.596	0.002	1.860-16.837

tal, and the data showed that the incidence rate of epilepsy after stroke reached 8.7%. Bladin et al. [7] conducted a multi-center case-control study in 2021 patients, and found 10.6% of epilepsy after hemorrhagic stroke and 8.6% of epilepsy after ischemic stroke in the patients. The results of our study were basically consistent with theirs, both suggesting high incidence of epilepsy after stroke. Therefore, it is essential to make additional studies on the risk factors for this disease and strategies for early intervention, with the aim to reduce the incidence of epilepsy after stroke. In our study, we explored the risk factors of epilepsy after acute cerebrovascular disease and found that epileptic seizure was associated with patients' cortical lesions, multi-lobar lesions, neurological severity score and symptoms of cardiogenic brain embolism, cerebral hemorrhage or cerebral infarction. Clinical studies reveal [8] that the probability of epilepsy after cortical hemorrhage is significantly higher than that of cortical lesions. Cortical lesions may be the essential cause for epilepsy after cerebral hemorrhage. Ming [9] also reported that the location of cortical infarction and stroke cardiogenic brain embolism were the major risk factors for early epileptic seizures. According to relevant international studies [10], one of the independent factors for status epilepticus (SE) is cardiogenic brain embolism. In this study, cerebral infarction, cerebral hemorrhage and cortical lesions were associated with the occurrence of epilepsy after cerebrovascular diseases and were also major risk factors for epileptic seizures. Epilepsy occurred in patients with cerebral hemorrhage may be attributed to biochemically functional disorders in nerve cells. Increases in hematoma stimulation and release of neurotransmitters may cause intracranial hypertension, resulting in a great deal of paradoxical discharge of the brain neurons in patients [11, 12]. Mechanisms of cortical infraction might be due to the fact that what in the cortex are mainly nerve cells and axons which are sensitive to discharging in the cortex, but few neurons are located in other parts of the body. Cardiogenic brain embolism is inclined to cause epileptic seizure which may be attributable to its rapid onset. Acute ischemia and hypoxia in case of unestablished collateral circulation in the brain tissues and cells may cause severe damages to the nerve cells in ischemia regions, resulting in injuries in the cortical branches of peripheral arteries and finally in epileptic seizures [13]. According to

relevant domestic studies, neurologic impairments are associated with epilepsy after stroke [14, 15]. Our study revealed the significantly higher incidence of epilepsy in patients with high neurological severity scores than in those with lower scores, and the difference was statistically significant. However, Martin et al. [16] reported that the severity of neurologic impairments was not associated with epileptic seizure in stroke patients. Their different findings may be due to the sampling errors and differences in regions and races. In our study, patients with cerebrovascular diseases presented the symptoms of multi-lobar lesions and had a higher risk of epileptic seizures, which is consistent with the findings reported in other related studies [17]. The multivariate Logistic regression analysis showed the associated factors such as cardiogenic brain embolism, cortical lesions, multi-lobar lesions and high neurological severity scores were major high risk factors for epilepsy after cerebrovascular diseases. The results were consistent with those reported in the other studies [18, 19].

This study did not cover the clinical features of patients with epilepsy after stroke. The selected patients were admitted in our hospital within a given period. Patients without hospitalization in our hospital were excluded, so there is a bias of selection.

Clinical patients were mostly elderly ones with declined memory, so there might be something wrong with the information on their previous physical conditions and medical history. Thus, there are a lot of confounding factors in this trial. The correlations between neurological severity score and this disease are controversial. Additional studies are needed to explore relevant specific mechanisms from the perspective of molecular biology, for the purpose of getting a better understanding of clinical diagnosis and treatment.

In conclusion, secondary epilepsy after stroke may be caused by a variety of etiological factors. Secondary epilepsy is a complication of cerebrovascular diseases, and epileptic seizure would aggravate cerebrovascular disease, thus resulting in a vicious circle [20]. Only with a better understanding of clinical pathogenesis of secondary epilepsy after cerebrovascular diseases and a thorough analysis on the pathogenic risk factors, can we make treatment and prevention targeted at the disease and decrease the incidence of secondary epilepsy. It also has implications for improving patients' recovery and quality of life in the future.

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