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Seizures after cerebrovascular events: Risk factors and clinical features

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ABSTRACT

Background: Epileptic seizures are well known sequelae of patients with stroke but only little is known about the different risk factors and about the influence of the different types of stroke including sinus thrombosis and bleedings on developing such seizures. Further, the association of post-stroke seizures and conventional vascular risk factors has not been evaluated to date.
Methods: We performed a cohort study on a sample of 593 consecutive patients with different types of cerebrovascular events. In 421 patients, sufficient data were obtained in a personal interview over a mean observation period of 30 months. Data regarding the clinical history were recorded from the patients' charts.
Results: The total prevalence of epileptic seizures was 11.6%, the total annual risk was 4.6%. We detected the following significant risk factors: younger age at stroke; higher NIH stroke scale score; any coagulopathy. TIA was found significantly less frequent as a cause of seizures as compared to infarction, bleeding, and sinus thrombosis. Patients with bleeding (14.3%) and with sinus thrombosis (16.3%) were significantly more frequent in the seizure group than in the non-seizure group (6.7% and 1.6%, respectively). The location of stroke, including cortical versus subcortical, did not influence the risk of seizures. The majority of patients developed secondary generalized seizures (57.1%). In adjusted analyses, the two major risk factors for post-stroke epilepsy were a higher NIH stroke scale and a sinus thrombosis as the initial cerebrovascular event. Common lifestyle, vascular, and metabolic risk factors of stroke and for dementia were not associated with the development of seizures.
Conclusions: In conclusion, our data show that epileptic seizures occur in particular after major strokes and in sinus thrombosis. Interestingly, conventional vascular risk factors were not associated with the occurrence of post-stroke seizures. Considering the risk for seizures after certain types of cerebrovascular events might help to early identify patients for anticonvulsive treatment. In the future, it should be investigated whether these patients might benefit from pre-emptive anticonvulsant treatment.

1. Introduction

Stroke is the most common risk factor for seizures in the elderly population accounting for 39–45% of all seizures.[1–3] In an ageing society and with further improvement in stroke treatment, it becomes crucial to find methods for the prevention of seizures which have considerable social and psychological impact on the patients.[4] Some epidemiological studies have been published regarding seizures after stroke but they differ in number of patients, inclusion criteria, time of follow up, and diagnostic methods. Many studies have examined intracerebral haemorrhage (ICH), subarachnoid haemorrhage (SAH), and ischaemic stroke. There is, however, not much data concerning the development of seizures after other cerebrovascular events including transient ischaemic attack (TIA), different types of bleeding, and intracranial venous thrombosis (IVT).[4] In this hospital-based study, we aimed to find risk factors that contribute to the development of seizures and epilepsy after stroke in patients with different types of cerebrovascular events in univariate and multivariate analyses.

2. Methods

We evaluated all patients admitted to the Stroke Unit of the Department of Neurology, University of Münster between January 2003 and March 2010 for whom sufficient data were available in the database ($n = 1611$). Out of this number, we selected all patients with a first ever ischaemic stroke, TIA, ICH, SAH, or IVT. Only strokes with cerebral manifestation were included; strokes in cerebellar or brain stem location were excluded. Patients who had died while they were still in hospital were also excluded.

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For the resulting 593 patients, a detailed questionnaire was completed. One part of the questionnaire (baseline demographic and clinical data) was filled in with data obtained from a patient chart review and a clinical interview with the patients who were in hospital between October 2009 and March 2010 with a minimum duration of 2 weeks after stroke. In the other patients, a follow-up telephone interview either with the patients themselves or with relatives on behalf of those patients who could not communicate was conducted at least 3 months after the initial event. Only cases with a successful interview were finally included in the study ($n = 421$). The mean time of follow-up was 30 months (maximum 78 months). In 172 cases, the follow-up interview could not be carried out for the following reasons: the patients had died meanwhile and no relative was available ($n = 21$); the contact data in the charts were not correct any more ($n = 139$); they did not want to participate for personal reasons ($n = 12$). At the time of interview, 41 patients (9.7%) had died but sufficient data was obtained by relatives. The flow chart of the different reasons for patients enrolled or excluded is presented in Fig. 1.

Seizures and epilepsies were classified according to the guidelines of the International League against Epilepsy (ILAE).[5,6] Early onset seizures were defined when they appeared within the first 7 days after stroke onset. Seizures were distinguished as being simple partial, complex partial, or generalized.

Stroke severity was measured using the National Institute of Health (NIH) stroke scale which was obtained on admission to the hospital. In all cases, a CT or MRI brain scan were performed to diagnose the type of stroke. TIA was defined as symptoms lasting less than 24 h and no correlation to the symptoms in MRI and CT. Ischaemic stroke was diagnosed via plain CT, CT-angiography, CT-perfusion studies, or MRI with diffusion-weighted-imaging (DWI); bleeding was diagnosed via CT and MRI with DWI. IVT was also diagnosed via CT angiography or MRI angiography. TOAST criteria classification of ischaemic stroke was confirmed by carotid Doppler and CT angiography for 'macroangiopathic stroke', by transoesophageal echocardiography for 'cardioembolic strokes', and by CT/MRI scan (stroke size less than 15 mm) and absence of significant findings in the other two diagnostic tools for 'microangiopathic stroke'. Further, events were classified as 'other defined aetiology' (e.g., cervical artery dissection) and of 'unknown origin' if none of the diagnostic approaches leads to inclusion in one of the aforementioned categories. Strokes were subclassified as having occurred in the anterior circulation if they occurred in the middle or anterior cerebral artery territory and in the posterior circulation if they had occurred in the vertebrobasilar territory. If a stroke had occurred in both it was excluded from this analysis in order to obtain homogenous subgroups. Only strokes clearly located in one of the two hemispheres were included in the respective analysis.

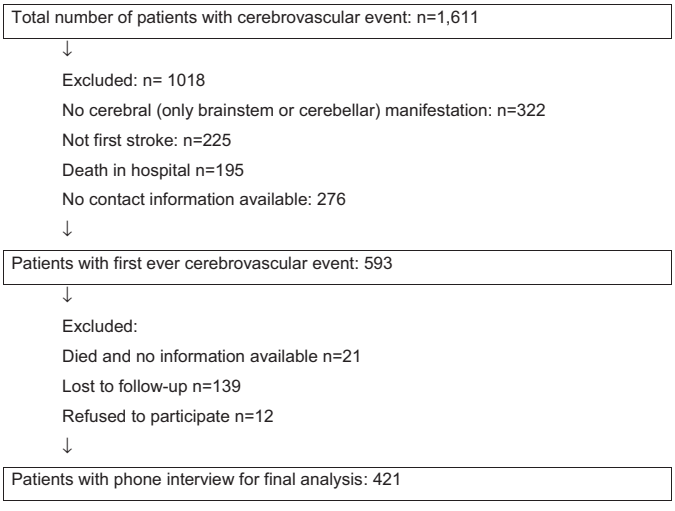

Fig. 1. Study flow chart of the enrolment.

Statistical analysis was performed using SPSS version 18. In the univariate analysis, categorical variables were compared using χ^2-test and Fisher's exact test (if applicable). For parametric variables, we described arithmetic mean and standard deviation. The significance of differences between two groups was tested by Mann–Whitney U test. For multivariate analysis, a logistic regression model (backward Wald) was used. For this model, we included factors that showed significant influence on seizure development in univariate analysis and allowed to test a group which was large enough to perform a logistic regression model. Significance level was set at $p = 0.05$.

3. Results

Out of the 421 patients finally enrolled, 53.2% ($n = 224$) were male and 46.8% ($n = 197$) were female. The mean age was 64.8 ± 15.1 years. In total, 9.7% ($n = 41$) had deceased at the time of the interview but sufficient data was available. The diagnoses were as follows: TIA, $n = 64$ (15.2%); ischaemic stroke, $n = 311$ (73.9%); ICH, $n = 32$ (7.6%); IVT, $n = 14$ (3.3%). Patients who developed secondary ICH were included with the original aetiology (ischaemic stroke/IVT). $N = 49$ patients (11.6%) developed at least one epileptic seizures. The patients' characteristics can be seen in Table 1. The calculated annual risk to develop a seizure was 4.6% for the total sample and 4.1% for ischaemic stroke.

The results of the univariate analysis for all variables regarded as potential risk factors for seizure development are presented in Table 2. Patients who developed seizures were significantly younger, had a significantly higher NIH stroke scale score, and received significantly more often an inpatient rehabilitation than patients without a seizure. Surprisingly, pre-existing cardiac conditions were significantly more frequent in patients without seizures than in patients with seizures. However, in the subgroup

Table 1
Characteristics of the total patients sample ($n = 421$).

Patients with at least one seizure	11.6%
Age (in years)	64.8 ± 15.1
Sex	
Female	46.8%
Male	53.2%
Lifestyle	
BMI	25.9 ± 4.1
Smoking (time of interview)	11.0%
Ex smokers	42.6%
Drinking alcohol (time of interview)	30.6%
Ex drinking alcohol	8.6%
NIH score	4.7 ± 5.1
Type of cerebrovascular event	
TIA	15.2%
Ischaemic stroke	73.9%
ICH	7.6%
IVT	3.3%
Type of ischaemic stroke (TOAST criteria)	
Cardiac origin	15.2%
Microangiopathic	4.8%
Macroangiopathic	20.6%
Other defined	6.4%
Unknown	38.9%
Multiple	14.5%
Cortical involvement of stroke	15.7%
Rehabilitation	
Ambulatory	5.5%
Inpatient rehabilitation	57.2%
No rehabilitation	37.3%

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