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Risk factors for post-stroke seizure recurrence after the first episode

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ABSTRACT

Purpose: Seizure is a common complication after stroke. However, the clinical characteristics, treatment, and recurrence rates in patients with the first episode of post-stroke seizure remain unclarified. The aim of this study was to identify the predictors of seizure recurrence in those patients.
Method: We retrospectively identified patients admitted to our hospital between July 2010 and June 2014 and followed-up until June 2015 because of the first episode of post-stroke seizure. We classified post-stroke seizure as early (within one week after stroke) or late (in the second week or later). We compared the baseline clinical characteristics and treatment between the groups and investigated the factors that determined seizure recurrence by Cox proportional hazards model.
Results: A total of 153 patients (84 men; mean age, 73.7 ± 12.3 years; 73 hemorrhagic and 80 ischemic strokes; 63 early and 90 late seizure) were included. Compared with the late seizure group, the early seizure group more frequently manifested with status epilepticus; tended to less often undergo stereotactic aspiration of hematoma; and less frequently used anti-epileptic drugs. During the observation period (median 364 days, IQR 124–680 days), 40 patients were lost to follow-up; subsequently, 113 patients were included in the analysis. The early seizure group had lower survival and seizure recurrence rates than the late seizure group. The factors significantly associated with seizure recurrence were presence of status epilepticus in the early group (HR 4.75, 95% CI 1.28–17.62) and younger age in the late seizure group (HR 0.95, 95% CI 0.93–0.99).
Conclusions: In patients with post-stroke seizure, status epilepticus and younger age were the predictors of recurrence after early and late seizure, respectively.

1. Introduction

According to the epidemiologic guidelines developed by the International League Against Epilepsy [1], first-episode seizures are divided into the acute symptomatic and unprovoked types. Acute symptomatic seizures occur in close relationship with an acute central nervous system insult, which may either be metabolic, toxic, structural, infectious, or inflammatory. Unprovoked seizures are defined as those occurring in the absence of a potentially responsible clinical condition or beyond the interval estimated for acute symptomatic seizures to occur. Unprovoked seizures differ from acute symptomatic seizures in terms of higher risk for recurrence and lower mortality rate [2].

Cerebrovascular disease is the most common cause of both acute symptomatic and unprovoked seizures in the elderly [3,4]. Post-stroke seizures (PSS) account for 39% to 45% of all seizures in the elderly [5,6]. According to previous reports [7], PSS occurring within 1 or 2 weeks after stroke are classified as early seizure (ES), whereas those occurring beyond that period are classified as late seizure (LS). Hemorrhagic stroke, high NIH stroke score, and cortical lesions are most commonly associated with PSS [7–12]. The risk factors for PSS recurrence have been reported to be late onset of seizure, stroke severity, age less than 74 years, valproic acid monotherapy, and the presence of convulsions on admission [9,13,14]. One report showed that young age and male gender were associated with seizure recurrence after the first post-ischemic stroke seizure [15]. Another report showed that a relatively large volume of hematoma was a predictor of seizure recurrence after the first post-hemorrhagic stroke seizure [16]. However, no reports have evaluated the risk factors for PSS recurrence after the first episode based on onset (ES vs. LS). In this hospital-based

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retrospective study, we sought to identify the predictors of seizure recurrence in patients with first-episode PSS based on timing of onset.

2. Methods

2.1. Study setting

All patients admitted to the Department of Stroke and Cerebrovascular Diseases of the National Cerebral and Cardiovascular Center (NCVC) were registered in a database (the NCVC Stroke Registry; Clinical Trials.gov: NCT02251665). The NCVC is a specialized and comprehensive cardiovascular center; data for the registry were collected systemically at the time of discharge.

We retrospectively identified patients with the first episode of PSS between July 2010 and June 2014 and who were followed-up until June 2015. We evaluated only those patients with sufficient available data from the hospitalization and outpatient records or from telephone inquiry with the patients or their relatives. Two stroke neurologists assessed the magnetic resonance imaging findings of the patients and evaluated cortical involvement. The diagnosis of PSS was made by stroke neurologists based on electroencephalogram findings and/or seizure semiology. Recurrence after the first episode of PSS was defined as readmission due to seizure. Symptoms that were not diagnosed definitely as seizure were excluded.

This study was approved by the ethics committee of the NCVC. Verbal consent for use of clinical records was taken from patients during follow-up. All data were anonymized prior to analysis. We disclosed the present study with an opt-out choice in our website.

2.2. Clinical characteristics, treatment, mortality, and seizure recurrence

We classified PSS into ES (within 1 week after stroke) and LS (in the 2nd week or later after stroke). The ES group comprised patients admitted in our hospital for stroke, after which the seizures occurred within one week. We compared the ES and LS groups in terms of baseline clinical characteristics, including age, sex, stroke type, status epilepticus, cortical involvement, cranial surgery (removal of hematoma and/or ventricular drainage in acute phase of stroke, before the first post-stroke seizure), and treatment. Status epilepticus was classified into convulsive and non-convulsive types. Convulsive status epilepticus was defined as a seizure lasting for more than 5 min or as more than one seizure episode within a 5-min period without returning to a normal state in between. Non-convulsive status epilepticus was defined as the persistent (>10 min) change in behavior and mental processes from baseline without motor symptoms [17]. The all diagnoses of non-convulsive status epilepticus required the epileptiform discharges and/or electroencephalogram findings and clinical improvement after intravenous anti-epileptic drugs (AED) [18]. History of treatment with AED was divided into two periods: acute phase (during hospitalization only) and maintenance phase (after discharge). Among patients with follow-up data, the ES and LS groups were compared in terms of rates of mortality and seizure recurrence. Seizure recurrence was defined as a seizure occurrence in the second week or later after the first episode. We investigated the factors that determined seizure recurrence in the ES and LS groups separately.

2.3. Statistical analysis

Continuous variables were presented as mean ± standard deviation or median and interquartile range (IQR). Differences in the clinical and demographic categorical variables between the ES and LS groups were evaluated by the Fisher's exact test. Mortality and seizure recurrence on the Kaplan–Meier curve were compared between the groups using the log-rank test. The predictors of seizure recurrence in each group were evaluated by the Fisher's exact test. The multivariate model included all parameters that had a p value of <0.25 on the Fisher's exact test. Cox proportional hazards regression models were used to evaluate the independent predictors of recurrence after the first episode of PSS. Results were presented as hazard ratio (HR) with 95% confidence interval (CI). All statistical tests were two-sided and p values of <0.05 were regarded as statistically significant. All statistical analyses were performed using JMP 11 (SAS Institute Inc. Cary, NC).

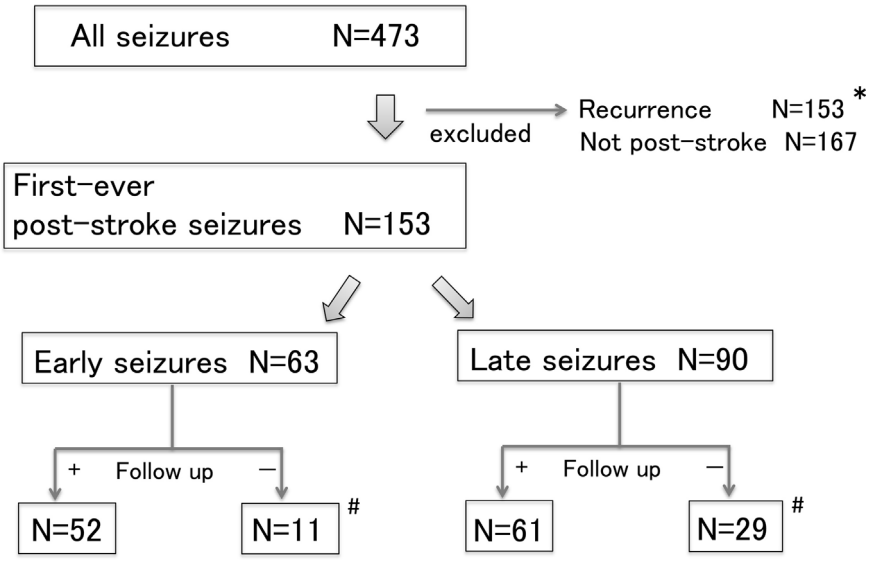

Fig. 1. Study design and protocol.
*Due to the fact that only patients with a first seizure episode after stroke were enrolled, we excluded 153 patients with recurrent post-stroke seizure and 167 patients with non-stroke seizure.
We could not follow-up 11 ES and 29 LS patients; this resulted to 40 insufficient data.