Journal of Clinical Neuroscience xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Opinion paper

Incidence of poststroke seizures: A meta-analysis

Lung Chan [a,b], Chaur-Jong Hu [a,b], Yen-Chun Fan [c], Fang-Yu Li [c], Han-Hwa Hu [a,b], Chien-Tai Hong [a,b,*,1], Chyi-Huey Bai [c,d,*,1]

[a] Department of Neurology, Shuang-Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
[b] Department of Neurology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
[c] School of Public Health, College of Public Health and Nutrition, Taipei Medical University, Taiwan
[d] Department of Public Health, School of Medicine, College of Medicine, Taipei Medical University, Taiwan

ARTICLE INFO

Article history:
Received 28 June 2017
Accepted 23 October 2017
Available online xxxx

Keywords:
Seizures
Stroke
Meta-analysis

ABSTRACT

Background: Late-onset poststroke seizure is highly associated with epilepsy but the incidence of it is variable due to different definition and follow-up time. We conducted a meta-analysis to determine the incidence of poststroke seizure and analyze the discrepancies among published studies.
Methods: We searched the literature for relevant articles published in English between January 1, 1990, and December 31, 2014, by using the following search terms: "seizures after stroke," "poststroke seizures," "epilepsy after stroke," "poststroke epilepsy," "incidence," and "follow-up." Reference lists of the relevant articles were reviewed to identify eligible studies not captured by these terms.
Results: Seven relevant cohort studies were identified and analyzed. Incidence density was defined as the number of episodes per 100 person-years. Using the definition of late-onset poststroke seizure as seizure occurring 14 days after a stroke, the incidence density was 1.12 (0.95–1.32) per 100 person-years. For poststroke seizures occurring 7 days after the stroke, the incidence density increased to 3.22 (2.94–3.52) per 100 person-years.
Conclusion: Our results are relevant to the epidemiology of late-onset poststroke seizure, with 14 days being the ideal cutoff time point. The pooled incidence density of late-onset poststroke seizure was 1.12 per 100 person-years in 4 cohort studies.

1. Introduction

Epilepsy is a common neurological disease. According to a World Health Organization survey, 50 million individuals have epilepsy worldwide; the majority of these cases are cryptogenic [1]. Among the etiologies of symptomatic epilepsy, stroke is the leading cause [2]; the stroke-damaged brain parenchyma easily becomes the epileptogenic focus, thus inducing epileptic seizures. Epilepsy considerably negatively affects the quality of life (QOL) of poststroke patients [3]. In addition, the detrimental drug–drug interactions of antiepileptic drugs interfere with the action of several crucial stroke prevention medicines, including antithrombosis, lipid-lowering, and blood pressure-controlling agents [4].

Several studies have investigated the characteristics of poststroke seizures and epilepsy. Severe stroke and cortical involvement are the common risk factors for poststroke seizures [5]. Some attacks occur very early after a stroke [6], whereas late-onset poststroke seizures more likely transform to epilepsy [7].

Some observational studies have reported the incidence of poststroke seizures and epilepsy. However, the lack of studies with a universal design limits the interpretation of their results with regard to the fundamental epidemiology of poststroke seizures and epilepsy. For instance, some studies define late-onset poststroke seizures as strokes occurring 1 week after a stroke, whereas others adopt a corresponding period of 2 weeks; this discrepancy leads to variation in the reported incidence [7–13].

Because poststroke seizures and epilepsy are vital issues for stroke patients, clarifying the incidence of poststroke seizure and epilepsy is crucial for improving public health. We therefore systemically searched the literature and meta-analyzed the identified studies to determine the incidence of poststroke seizure and epilepsy and analyze the discrepancies among the studies.

* Corresponding authors at: Department of Neurology, Shuang-Ho Hospital, Taipei Medical University, New Taipei City, Taiwan (C.-T. Hong). School of Public Health, College of Public Health and Nutrition, Taipei Medical University, 5/F Health Science Building, 250 Wu-Hsing Street, Taipei City 110, Taiwan (C.-H. Bai).
E-mail addresses: cjustinmd@tmu.edu.tw (L. Chan), chaurjongh@tmu.edu.tw (C.-J. Hu), ct.hong@tmu.edu.tw (C.-T. Hong), baich@tmu.edu.tw (C.-H. Bai).
[1] Chien-Tai Hong and Chyi-Huey Bai contributed to this study equally.

https://doi.org/10.1016/j.jocn.2017.10.088
0967-5868/

2. Methods

2.1. Literature search strategy

All relevant articles published in English between January 1, 1990, and December 31, 2014, were identified by searching PubMed, BioMed Central, Medline, and Google Scholar. The search terms were as follows: "seizures after stroke," "poststroke seizures," "epilepsy after stroke," "poststroke epilepsy," "incidence," and "follow-up." Moreover, the reference lists of the relevant articles were reviewed to identify eligible studies not captured by these search terms. A flow chart of our literature search is shown in Fig. 1. Finally, 87 full-text articles were identified.

2.2. Inclusion and exclusion of literature

The inclusion criteria were as follows: (1) clear definition regarding stroke diagnosis and types; (2) clear definition regarding the diagnosis of seizures or epilepsy; (3) no inclusion of mixed episodes of seizures; (4) cohort study or follow-up study published as an original article; (5) sample size of studied population ≥200 persons; (6) clear records regarding follow-up duration, such as start and end dates; (7) adequate information regarding seizures or epileptic episodes separated at 0–7, 7–14, and 14–365 days after a stroke; (8) availability of episode number and follow-up person-time; and (9) published in English. Only 7 articles satisfied the inclusion criteria.

2.3. Data extraction

The following information was extracted: first author name; publication year; country and location; study design; diagnostic criteria for stroke and seizures or epilepsy; number of cases or sample size and person-time separated at 0–7, 7–14, and 14–365 days after a stroke; sex; and mean age at baseline (years). All data were independently reviewed by 3 investigators (BAI CH, LI FU, and FAN YC), and their disagreements were resolved through consensus. The data from the 7 candidate articles were independently extracted by two investigators (BAI CH and FAN YC).

2.4. Statistical analysis

The follow-up person-time was calculated separately at 0–7, 7–14, and 14–365 days after the stroke. The seizures or epileptic episodes were also aggregated by onset time. The aggregated results were calculated using the incidence density method and weighted by sample size. The 95% confidence intervals of the incidence density were calculated on the basis of a binomial assumption. I^2 was used to assess heterogeneity across studies. All statistical analyses were performed using SAS software (version 9.3; Statistical Analysis System, SAS.com, USA). All reported probability (P) values were two-sided, with $P < .05$ considered statistically significant.

3. Results

Fig. 1 summarizes our process of identifying the eligible observational studies. After searching PubMed, BioMed Central, Medline, and Google Scholar, 87 full-text articles published during January 1990–December 2014 were selected for eligibility assessment. We excluded articles with unclear stroke and seizures definitions and unclear follow-up details, articles pertaining to noncohort studies, and articles irrelevant to our study topic. Sixteen articles satisfied the aforementioned criteria and were subjected to qualitative synthesis. Nine of these studies were excluded because of nonseparation by 14 days after a stroke or mixed episodes of seizures, thus yielding a final study sample of only 7 cohort studies.

3.1. Study characteristics

The characteristics of the included cohorts are summarized in Table 1. The total number of stroke patients was 4474. The studies were conducted worldwide, including in North and South America, Europe, Asia, and Oceania [7–13].

Lancman et al. followed 219 consecutive ischemic or hemorrhagic stroke patients for an average of 11.5 months (range 1–72 months). They defined the early- and late-onset poststroke seizures as those occurring during and after the first month following the stroke, respectively; 22 (10.04%) patients had poststroke seizures–12 early onset and 10 late onset [10].

Three years later, So et al. reported the following: 535 consecutive persons without prior unprovoked seizures were followed from their first cerebral infarction until death or migration out of Rochester, Minnesota, USA (follow-up duration: 5.5–7.1 years). Unprovoked seizures developing beyond 1 week after cerebral infarction were defined as late poststroke seizures, whereas poststroke epilepsy was defined as recurrent late poststroke seizures. Twenty-seven (5.0%) developed late poststroke seizures, whereas 18 (3.4%) developed poststroke epilepsy [13].

Bladin et al. conducted a multicenter prospective cohort study to investigate poststroke seizures and epilepsy; 2021 consecutive patients with acute stroke admitted to university teaching hospitals with established stroke units were studied. After excluding 124 patients with previous epilepsy or without computed tomographic diagnosis, 1897 patients were analyzed, with a mean follow-up duration of 9 months. Seizures occurred in 168 (8.9%) of these stroke patients, and epilepsy developed in 47 (2.5%) patients. In other words, 28% of the poststroke seizure patients transformed to poststroke epilepsy [8].

Dhanuka et al. conducted a prospective study on poststroke seizure in India among 269 consecutive stroke patients studied with a mean follow-up of 15.9 months; 35 (13%) patients were diagnosed with poststroke seizures [9].

Lamy et al. conducted a study focused on poststroke seizures in young adults with cryptogenic stroke. In total, 581 patients with recent cryptogenic ischemic stroke were prospectively enrolled, with a follow-up of 37.8 ± 9.7 months. Twenty (3.4%) patients developed unprovoked seizures beyond 1 week after a stroke [11].

Naess et al. investigated the long-term outcome of young stroke patients and revealed that among 232 stroke patients aged 15–49 years, 20 (8.8%) had seizures 7 days after a stroke. The mean follow-up duration was 5.7 years [12].

The most recent cohort study was published by Arntz et al. It was a prospective cohort study enrolling 697 consecutive young patients with a first-ever stroke including transient ischemic attack, ischemic stroke, and intracranial hemorrhage. The mean follow-up was of 9.1 years, and 54 (7.7%) patients developed poststroke seizure 7 days after a stroke [7].

3.2. Incidence density of poststroke seizure

To resolve the discrepancy in the follow-up durations among the studies, we used the incidence densities to pool the study results. Incidence density is defined as the number of events per 100 person-years. We pooled 4 studies that defined late-onset poststroke seizure as that occurring 14 days after a stroke together. The resultant incidence density was 1.12 (0.95–1.32) per 100 person-years (total 139 events in 12400.8 person-years; Fig. 2).

Shortening the definition of late-onset poststroke seizure to 7 days after a stroke enabled the pooling of the incidence densities of all 7 studies. The incidence density increased to 3.22

Please cite this article in press as: Chan L et al. Incidence of poststroke seizures: A meta-analysis. J Clin Neurosci (2017), https://doi.org/10.1016/j.jocn.2017.10.088