Prognostic analysis for short- and long-term outcomes of newly diagnosed epilepsy

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ABSTRACT

Purpose: To explore predictors for short- and long-term prognosis of newly diagnosed epilepsy.
Methods: 549 consecutive patients with newly diagnosed epilepsy were reviewed, 336 were enrolled in the study. Two-year remission in the short term (5 years) and five-year remission in the long term (>5, up to 8 years) were assessed as the outcomes. Logistic regression was used to identify independent predictors for unfavorable outcomes. χ^2 test was used to compare the retention rates of old and new antiepileptic drugs (AEDs).
Results: 185 patients (55%) attained two-year remission in the short term, 163 (48.5%) attained terminal remission in the long term. The time interval between index seizure and AED start >12 months implied an unfavorable outcome in the short term (OR = 1.9, p = 0.03). Two or more seizures in the first year after AED start showed the strongest negative prognostic impact in the both short- and long-term outcomes (OR = 2.3, p = 0.02; OR = 1.9, p = 0.03). As the seizure frequency rose, the possibility for unfavorable outcome increased. The terminal retention rates of traditional and new AEDs were not significantly different (p = 0.07).
Conclusions: For patients with newly diagnosed epilepsy, the time interval between index seizure and AED start only influences the short-term outcome. Number of seizures in the first year after AED start is associated with both short- and long-term outcomes. It's imperative to initiate adequate, tolerated and appropriately chosen AED schedules after the definitive diagnosis of epilepsy.

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1. Introduction

As one of the most prevalent chronic neurological condition characterized by the recurrence of unprovoked seizures, epilepsy is afflicting seventy million people worldwide, with 50.4 per 100,000 people newly diagnosed every year [1]. In clinical practice, the final goal of epilepsy management is to help patients attain complete seizure freedom with the minimal side effects of antiepileptic drugs (AEDs) [2]. Previous studies have indicated that the high frequency of seizures before appropriate AEDs therapy, poor response to initial AEDs therapy, specific epilepsy syndromes might suggest a worse outcome [3–5]. However, early predictors for short- and long-term outcomes of newly diagnosed epilepsy, which are crucial to guide timely AEDs therapy, are still partially unsettled.

Based on a pre-set epilepsy database, we conducted a retrospective study to explore potential risk factors associated with the short- and long-term prognosis of newly diagnosed epilepsy. The retention status of AEDs at the end of follow-up was also presented in the study.

2. Methods

2.1. Patients and setting

This retrospective cohort study is based on the detailed documentations in the database of the epilepsy clinic in the Xijing Hospital, a tertiary academic medical care center and one of the largest hospitals in western China. Between January 2008 and December 2010, 549 consecutive outpatients with newly diagnosed epilepsy and without histories of AEDs intake before the first appointment were reviewed. Epilepsy and epileptic seizure are defined according to the consensus carried out by The International League Against Epilepsy (ILAE) in 2014 [6]. The etiologies of epilepsy were classified into three categories idiopathic, symptomatic, or cryptogenic. The patients with symptomatic epilepsy

were further grouped into: central nervous system (CNS) infection, traumatic brain injury, cortical dysplasia, vascular, and others (etiologies other than those above mentioned were classified as "others"). All the patients in the study were diagnosed and treated by the same neurologist. This study was approved by the ethics committee of the Xijing Hospital and was carried out in agreement with Chinese laws and the Declaration of Helsinki. All subjects participating in the study provided informed consent.

2.2. Variables

After each patient's appointment, trained research assistants entered all the pertinent data into an electronic database. Based on this pre-set epilepsy database, the following data were collected: demographic and clinical characteristics, seizure history, AED medications and seizure trajectories, side effects, and assistant examination results. The time interval between index seizure and AEDs start was evaluated and categorized into four groups: 0–6 months, 6–12 months, 12–60 months and >60 months. Index seizure was defined as the seizure that caused the patient to be registered in this study, which resulted in the diagnosis being made. The seizure frequency before the first appointment was defined as mean seizure density in one year before the first appointment. The number of seizures in the first year after AEDs start were recorded and stratified into 3 categories (0–1; 2–5; >5). Status epilepticus was defined as continuous seizure activity or not regaining consciousness between seizures for at least 5 min [7]. A continuous video-EEG (≥ 15 h) was performed in each patient before initiating AED therapy. EEG characteristics were dichotomized into epileptiform activity (spikes, sharp waves, or spike-wave complexes) and absent epileptiform activity (normal EEG or slow waves). Neuroimaging examinations (MRI or CI) performed on admission and within one year after admission were collected, and the worst results were recorded. According to whether the abnormality potentially induces seizures or not, neuroimaging characteristics were dichotomized into two groups.

2.3. Outcome assessment

A median follow-up of 6.0 years (IQR, 5.3–7.6) was performed in 549 patients and ended on December 31, 2015. Patients with poor compliance were excluded. A PDC (proportion of days covered) <0.80 was considered as poor compliance [8]. Short-term (5 years) and long-term outcomes (>5 years up 8 years) were assessed based on the data recorded in the epilepsy database and telephone interview by a trained research assistant who was blinded to the clinical data entered during the first year of initial AED therapy. Outcomes were assessed according to whether 2-year remission was attained in the short term and whether 5-year remission was attained in the long term.

2.4. AED medication investigation

The main reasons for the treatment failure (withdrawal of the initial AED, added or replaced by another AED) were explored from the following aspects: lack of efficacy (LE), adverse events (AEs), and others (pregnancy, poor economic conditions, non-compliance). Retention rates of traditional and new AEDs were calculated at the end of follow-up. According to the chronological introduction order of those AEDs in China, we grouped valproic acid (VPA), carbamazepine (CBZ), phenytoin (PHT) and phenobarbitone (PB) as old AEDs, which were introduced to Chinese market before 2000, while levetiracetam (LEV, 2006), lamotrigine (LTG, 2007), oxcarbazepine (OXC, 2006), topiramate (TPM, 2007) were classified into new AEDs group.

2.5. Statistical analysis

Continuous variables were presented as mean $\pm$ standard deviation (normally distributed), as median and interquartile ranges (IQR, not normally distributed). Univariate and multivariate logistic regressions were used to screen and examine potential risk factors associated with the unfavorable outcome of newly
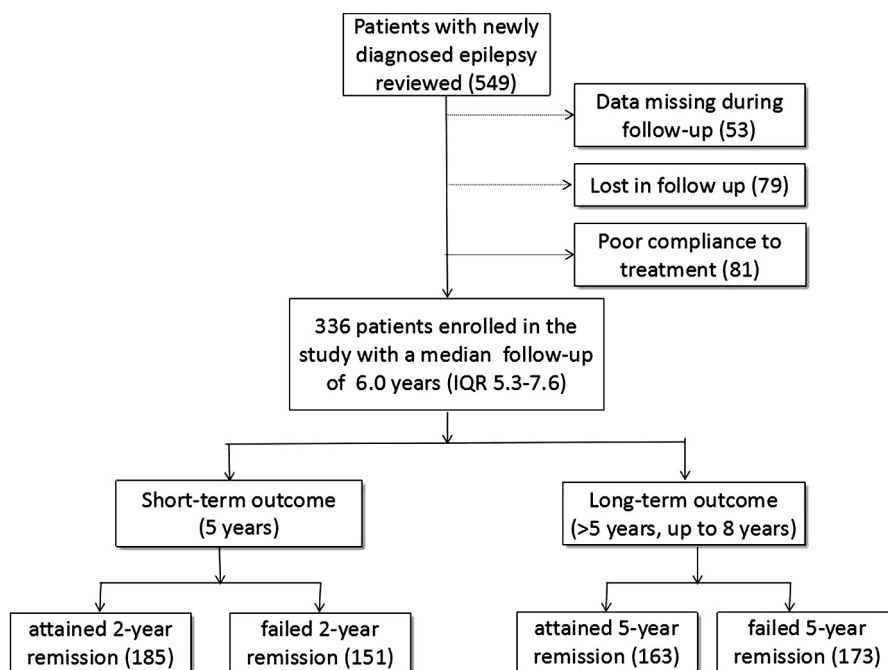

Fig. 1. Flow diagram of the study.