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### **Epilepsy & Behavior**

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

# Is antiepileptic drug withdrawal status related to quality of life in seizure-free adult patients with epilepsy?



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#### ARTICLE INFO

Article history: Received 14 November 2013 Revised 27 November 2013 Accepted 29 November 2013 Available online 7 January 2014

Keywords: Epilepsy Quality of life Seizure-free Withdrawal Determinant

#### ABSTRACT

*Purpose:* This study aimed to determine factors that influence the quality of life (QOL) of seizure-free adult patients with epilepsy in western China and address whether these determinants vary by antiepileptic drug (AED) withdrawal.

*Methods:* A cross-sectional study was conducted in the epilepsy outpatient clinic of West China Hospital, Sichuan University. Patients with epilepsy who were aged at least 18 years and seizure-free for at least 12 months were interviewed using the Quality of Life in Epilepsy Inventory-31 (QOLIE-31); the National Hospital Seizure Severity Scale (NHS3); the Liverpool Adverse Events Profile (LAEP); the Social Support Rating Scale (SSRS); the Family Adaptation, Partnership, Growth, Affection, and Resolve (APGAR) Questionnaire; and the Scale of Knowledge and Attitudes Toward Epilepsy. Eligible patients were divided into two groups: the nonwithdrawal group and the withdrawal group. The independent-samples *t*-test was used to compare the QOL between the groups, and linear regression analysis was used to explain the variance of their QOL

*Results:* One hundred and eighty-seven (135 nonwithdrawal and 52 withdrawal) patients were included in the analysis. The QOLIE-31 overall score of the nonwithdrawal group was lower than that of the withdrawal group (p < 0.01). The LAEP score was the strongest predictor of the QOLIE-31 overall score of all subjects, explaining 26.9% of the variance. The second strongest predictor was the SSRS score, explaining 12.9%, and the other predictors were the NHS3 score (5.2%), education level (2.3%), age (1.5%), and marriage (1.0%). Furthermore, the strongest predictors in the nonwithdrawal group were the LAEP and SSRS scores, while in the withdrawal group, the strongest predictors were stigma scores and employment.

*Conclusion:* Among the seizure-free adult patients with epilepsy, those with AED withdrawal experienced better QOL than those continuing AED treatment. Furthermore, the determinants of QOL varied by AED withdrawal. Individual strategies to optimize QOL should be developed based on these differences.

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#### 1. Introduction

Epilepsy is not merely a common chronic neurological disorder [1]; it is also a disorder with negative social consequences [2]. People with epilepsy are reported to experience reduced quality of life (QOL) [3], which could be influenced by many factors, including demographics, seizure-related factors, medications, and psychosocial variables [4–8]. Furthermore, when compared to people with other chronic conditions such as asthma and diabetes mellitus, people with epilepsy report worse QOL [9,10]. Therefore, improving the QOL of people with epilepsy is generally the most important goal of epilepsy management and the dominant focus in the care of patients with epilepsy.

Based on the evidence indicating that seizure frequency plays a critical role in the QOL of people with epilepsy [11,12], the determinants of

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QOL in seizure-free patients with epilepsy may differ from those in active epilepsy. On the other hand, although epilepsy is a relatively benign condition that may be well controlled for most patients [13,14], the OOL of seizure-free adult patients with epilepsy has been investigated in but a few studies [15-17]. This results in less knowledge related to these patients' QOL, and the factors that are the strongest predictors of QOL among seizure-free adult patients with epilepsy remain unclear. Furthermore, to our knowledge, there are no specific guidelines on AED withdrawal in seizure-free adults with epilepsy on the basis of current knowledge; deciding to discontinue drug therapy for the adult patients with a prolonged period of seizure freedom remains controversial. Consequently, the QOL of seizure-free adult patients with epilepsy with AED withdrawal is often not considered, and there is only a limited number of published studies examining their QOL [17]. Additionally, whether drug withdrawal increases QOL remains controversial. Accordingly, to optimize QOL in these patients, it is necessary to illuminate the main determinants of QOL and investigate the influence of drug withdrawal.

Therefore, in the present study, we investigated the QOL among adult patients with epilepsy who had been seizure-free for at least 12 months and identified the most relevant predictors of their QOL. We also





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examined the influence of AED withdrawal on QOL in these patients. Moreover, we speculated that the determinants may vary by drug withdrawal.

#### 2. Methods

#### 2.1. Participants

All participants in this cross-sectional study were recruited from the epilepsy outpatient clinic in West China Hospital, Sichuan University and consecutively enrolled from July 2011 to December 2012. All subjects had a confirmed diagnosis of epilepsy based on the International League Against Epilepsy criteria published in 1989 [18]. Eligible patients were at least 18 years of age and had been seizure-free for at least 12 months before enrolling in the study. Patients were excluded if they had an intellectual disability or any other reason for being unable to complete the study questionnaires. The study was approved by the Ethics Committee of West China Hospital, Sichuan University, and written informed consent was obtained from all of the participants.

#### 2.2. Clinical information and demographic status

Participants' clinical information was obtained from medical records, and the demographic characteristics that potentially influence QOL, including the patient's age, gender, education level, marriage status, and employment status, were obtained during the interview. Patients were divided into two groups according to whether they experienced AED withdrawal: the nonwithdrawal group and the withdrawal group.

#### 2.3. Measurements

Quality of life was measured using a widely adopted epilepsyspecific QOL instrument, the Quality of Life in Epilepsy Inventory-31 (QOLIE-31) [19]. A Chinese version of the QOLIE-31, which has been shown to be a valid and reliable questionnaire in assessing QOL in Chinese people with epilepsy [20,21], was used in our study. This measure consists of 31 questions divided into seven domains: Seizure Worry, Overall QOL, Emotional Well-Being, Energy/Fatigue, Cognitive Functioning, Medication Effects, and Social Functioning. Each domain was scored by calculating the mean score of the responses to the questions within that domain. The total score was calculated by assigning different percentages to the seven scores, ranging from 1 to 100. Question 31 is a subjective assessment of one's general health condition and was not included in the total QOL score.

Perceived AED side effects were assessed using the Chinese version of the Liverpool Adverse Events Profile (LAEP) [22]. It comprises 22 items investigating the frequency of the most common adverse effects of AEDs during the previous four weeks on a four-point Likert scale. A global summary score ranging from 22 to 88 was calculated; higher scores indicate a greater burden of adverse effects.

Seizure severity was assessed using the National Hospital Seizure Severity Scale (NHS3) [23], which contains seven seizure-related factors and generates a score from 1 to 27.

The perceived rate of social support received by patients was evaluated using the validated version of the Chinese Social Support Rating Scale (SSRS), which was originally developed in Chinese by Xiao [24]. This scale consists of 10 items, and higher scores indicate more social support.

Satisfaction with family support was assessed using the Family Adaptation, Partnership, Growth, Affection, and Resolve (APGAR) Questionnaire [25], which collects information on satisfaction with the aforementioned five areas of family function and consists of five statements. Scores on this instrument range from 0 to 10, and higher scores indicate greater family support. Patients' perceived stigma of epilepsy was measured using the Scale of Knowledge and Attitudes Toward Epilepsy, of which five extraction items address perceptions related to the epilepsy stigma [26]. Participants were asked about how much they agreed with the statements that people with epilepsy were dangerous and that it was possible to tell if a person had epilepsy by looking at him or her. To answer these questions, participants were given the following options: strongly agree, agree, disagree, strongly disagree, and do not know. To the other three item - whether they thought epilepsy would make someone unpopular, whether they thought epilepsy would lead to being picked on or bullied more by others, and whether they would date a person with epilepsy - participants were asked to respond with one of the following options: yes, not sure, no, and do not know about epilepsy. The highest possible overall score of 5 reflects the highest degree of perceived stigma.

#### 2.4. Statistical analysis

Data processing and analysis were conducted using SPSS version 17.0 (SPSS Inc., Chicago, Illinois) for Windows. All outcome variables were summarized using descriptive statistics. Quantitative data were expressed as the mean  $\pm$  SD, and gualitative data were summarized as proportions. A Pearson chi-square test and an independent-samples *t*-test were used to test between-group differences for the categorical variables and mean values of the data, respectively. Multivariate linear regression analyses were performed to explore the association between the possible determinants of QOL (independent variables) and the OOLIE-31 overall and subscale scores (dependent variables), in which the independent variables were included using stepwise selection (entry criterion of probability  $p \le 0.05$ , exit criterion of probability p > 0.1). The adjusted R<sup>2</sup> was used to assess the rate of variance of the domain score explained by the full model. Squared semipartial correlations were calculated to estimate the unique contribution of each independent variable to the variance in QOLIE-31 scores. A "p" value < 0.05 was considered statistically significant.

#### 3. Results

#### 3.1. Demographic and clinical characteristics

Complete data were available for 187 (135 nonwithdrawal and 52 withdrawal) patients (Table 1). The mean age for all of the subjects was  $30.57 \pm 10.75$  years. Eighty-one (43.3%) patients were female. Ninety-nine (52.9%) patients were married. Of all participants, approximately 40% had received higher education (including college and university), and approximately 70% were employed. The mean onset age was  $21.04 \pm 11.25$  years, and the mean duration of epilepsy was  $9.62 \pm 5.84$  years. Seventy-seven percent (144 patients) of all patients experienced generalized tonic-clonic seizures (GTCS) (including primary and secondarily GTCS).

No statistically significant differences were observed between the nonwithdrawal and withdrawal groups with respect to the above demographic variables and clinical characteristics (Table 1) (p < 0.05).

#### 3.2. QOLIE-31 scores

The mean QOLIE-31 overall score for all 187 patients was  $86.34 \pm 10.71$  (Table 2), and the mean subscale scores ranged from  $78.44 \pm 13.16$  for the Overall QOL to  $92.39 \pm 10.61$  for Emotional Well-Being. The mean scores for the remaining subscales were the following:  $88.82 \pm 16.30$  (Seizure Worry);  $91.18 \pm 11.46$  (Energy/Fatigue);  $85.83 \pm 11.86$  (Cognitive Functioning);  $79.70 \pm 23.18$  (Medication Effects), and  $85.19 \pm 18.91$  (Medication Effects).

The mean QOLIE-31 overall score and the mean of each of the seven subscale scores were lower in the nonwithdrawal group than those in

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