



Predictors of quality of life and their interrelations in Korean people with epilepsy: A MEPSY study



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ABSTRACT

Purpose: People with epilepsy (PWE) are more likely to have impaired quality of life (QOL) than the general population. We studied predictors of QOL and their interrelations in Korean PWE.

Methods: Subjects who consecutively visited outpatient clinics in four tertiary hospitals and one secondary care hospital were enrolled. These subjects completed the Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E), the Generalized Anxiety Disorder-7 (GAD-7), the Quality of Life in Epilepsy-10 (QOLIE-10), and the Korean version of Liverpool Adverse Event Profile (K-LAEP). We evaluated the predictors of QOL by multiple regression analyses and verified the interrelations between the variables using a structural equation model.

Results: A total of 702 PWE were eligible for the study. The strongest predictor of the overall QOLIE-10 score was the K-LAEP score ($\beta = -0.375$, $p < 0.001$), followed by the K-NDDI-E score ($\beta = -0.316$, $p < 0.001$), seizure control ($\beta = -0.152$, $p < 0.001$), household income ($\beta = -0.375$, $p < 0.001$), and GAD-7 score ($\beta = -0.119$, $p = 0.005$). These variables explained 68.7% of the variance in the overall QOLIE-31 score. Depression and seizure control had a bidirectional relationship and exerted direct effects on QOL. These factors also exerted indirect effects on QOL by provoking adverse effects of AEDs. Anxiety did not have a direct effect on QOL; it had only indirect effect through the adverse effects of AEDs.

Conclusion: Depression, anxiety, seizure control, and adverse effects of AEDs have complex interrelations that determine the QOL of PWE.

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Abbreviations: PWE, people with epilepsy; QOL, quality of life; AED, antiepileptic drug; TLE, temporal lobe epilepsy; WCE, well-controlled epilepsy; PCE, poorly controlled epilepsy; UCE, uncontrolled epilepsy; PDD, prescribed daily dose; DDD, defined daily dose; K-NDDI-E, Korean version of the Neurological Disorders Depression Inventory for Epilepsy; GAD-7, Generalized Anxiety Disorder-7; K-LAEP, Korean version of Liverpool Adverse Event Profile; QOLIE-10, Quality of Life in Epilepsy-10; NFI, Normed Fit Index; CFI, Comparative Fit Index; GFI, Goodness of Fit Index; RMR, root mean-square residual; LSSS, Liverpool Seizure Severity Scale; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; SCID, Structured Clinical Interview for DSM-IV axis I disorders.

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1. Introduction

People with epilepsy (PWE) appear to have poorer quality of life (QOL) than the general population not only because of the seizures but also because of comorbid conditions such as medical, psychiatric, and psychosocial problems.¹ Moreover, when PWE take an antiepileptic drug (AED) for a period of time, that drug can elicit adverse effects that further impair their QOL.² For these reasons, the identification of predictors of reduced QOL in PWE is critical for improving the targeting and optimization of existing and emerging interventions and management strategies for epilepsy.³

Predictors of QOL in PWE have been thoroughly summarized in a systematic review from the UK.³ This review included 93 QOL studies that were identified by Medline, Embase, and Cochrane Library searches up to July 2010. Increases in seizure frequency, seizure severity, levels of depression, levels of anxiety, and the

presence of comorbidities were strongly associated with reduced QOL. However, age, gender, marital status, type of seizure, age at diagnosis, and duration of epilepsy were found to be unlikely to be associated with QOL. The predictive values of educational and employment statuses, the number of AEDs and the adverse effects of AEDs for QOL were not determined.

Many studies have consistently reported that the strongest predictors of QOL in PWE are depression and anxiety among various other factors.^{4–9} Depression and anxiety have been found to be better predictors that seizure control or the adverse effects of AEDs. However, some studies have reported that other variables have the greatest predictive values. An Italian, multicenter study of people with pharmaco-resistant epilepsy reported that the adverse effects of AEDs were the strongest predictor, followed by depression symptoms, pharmaco-resistance grade, age, and lack of a driving license.¹⁰ A hospital-based, Chinese study of people with various seizure frequencies also reported the adverse effects of AEDs were the strongest predictor, followed by the number of AEDs, depression symptoms, and anxiety symptoms.¹¹ A hospital-based, Russian study found seizure frequency to be a stronger predictor of QOL than depression; indeed, seizure frequency was found to be the strongest predictor in that study.¹²

Therefore, the factor with the strongest influence on QOL in PWE has yet to be elucidated.

Depression and anxiety, the adverse effects of AEDs, and seizure control are related to each other. Regarding the relationship between seizure control and depression and anxiety, people with drug-refractory epilepsy have been reported to exhibit higher frequencies of depression and anxiety than those with well-controlled epilepsy.^{13,14} Regarding the relationship between the adverse effects of AEDs and depression and/or anxiety, PWE, depression and anxiety, even those presenting with subsyndromic types, are more likely to experience adverse effects of AEDs than those without these disorders.¹⁵ People with pharmaco-resistant epilepsy also exhibit higher frequencies of adverse effects of AEDs when they also have depression symptoms.¹⁰ Regarding the relationship between seizure control and the adverse effects of AEDs, seizure control is one of predictors of adverse effects of AEDs in PWE.^{16,17} Taken together, these results suggest that complex interrelations between these variables and their contributions to QOL likely exist.

The interrelations between the predictors of QOL in PWE have not been well studied. In an Asian, hospital-based study, the interrelations between the variables in terms of their contributions to QOL were clarified in PWE.⁴ Depression, anxiety, seizure control, the number of AEDs, and sleep disturbances had complex interrelations in their contributions to QOL as documented by a structural equation model. However, due to the relatively small sample size, only a limited number of variables could be examined in this study. For example, socioeconomic status, the adverse effects of AEDs, the underlying epilepsy syndrome, and the seizure focus were not considered as variables. Therefore, our aims were to perform a cross-sectional study to determine the predictors of QOL in a large sample of PWE and to clarify their interrelations.

2. Methods

2.1. Subjects

We invited subjects who consecutively visited the epilepsy clinics of secondary and tertiary care hospitals. The subjects were adults between the ages of 20–70 years with current diagnoses of epilepsy who had taken one or more AEDs for at the year prior to recruitment and were capable of providing informed consent and agreeing to the study protocol. Subjects with insufficient information in their medical records, with mental retardation or

serious medical, neurological, or psychiatric disorders that prevented them from understanding the questionnaire and cooperating with the study, and those who declined to complete the questionnaires were excluded.

2.2. Study design

The multicenter trial of epilepsy and psychiatric diseases (MEPSY) is a multicenter, cross-sectional study assessing depression, anxiety, suicidality, the burden of the adverse effects of AEDs, and the quality of life of Korean PWE. The subjects were enrolled consecutively beginning in November 2012 at the outpatient epilepsy clinics of four tertiary and one secondary care hospitals in Daegu city, which located in the southern part of Korea. This study was performed as a part of the MEPSY study. The institutional review board of each center approved the study, and all subjects provided written informed consent before participating in the study. The subjects were diagnosed according to the ILAE classification of seizures and epileptic syndromes.^{18,19} All patients were interviewed by trained epileptologists who also reviewed the subjects' medical charts to collect demographic, socioeconomic, and clinical information, which was entered into a computerized database. The socioeconomic variables included the following: having a job versus not having a job; earning at least one million Korean won (KRW) per month (equivalent to US\$ 900 per month) versus earning less than one million KRW per month; having a driving license versus not having a driving license; and being married versus being divorced, bereaved, or unmarried. The clinical variables included the following: age at onset, disease duration, seizure type, etiology, epilepsy syndrome, seizure control, MRI abnormality, history of febrile convulsion, family history of epilepsy, duration of AED intake, AED therapy regimen, and AED load. We divided the etiologies into idiopathic/cryptogenic and symptomatic epilepsy. We divided the epileptic syndromes into four groups: temporal lobe epilepsy (TLE), extraTLE, generalized epilepsy, and unknown syndromes. extraTLE included epilepsy syndromes in which the epileptic attacks originated from the frontal, parietal, or occipital lobes. We also divided seizure control into three groups: well-controlled epilepsy (WCE), poorly controlled epilepsy (PCE), and uncontrolled epilepsy (UCE). WCE was defined by freedom from seizures over the preceding year. UCE was defined according to the criteria used to determine drug-refractory epilepsy (i.e., the failure of adequate trials of two AEDs, an average of more than one seizure per month for 18 months and no seizure-free periods longer than three months²⁰). PCE was defined as an intermediate degree of seizure control that did not meet the criteria for WCE or UCE. The seizure control classification for each PWE was determined based on information about seizure frequency that was obtained from the medical records. The AED load of each individual patient was estimated as the sum of the prescribed daily dose (PDD)/defined daily dose (DDD) ratios for each AED included in the treatment regimen²¹ where DDD corresponds to the assumed average maintenance daily dose of a drug that is used for its main indication.²²

Eligible subjects completed several self-report questionnaires that included the Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E),²³ the Generalized Anxiety Disorder-7 (GAD-7),²⁴ the Korean version of the Liverpool Adverse Event Profile (K-LAEP),¹⁷ and the Quality of Life in Epilepsy-10 (QOLIE-10).²⁵

2.3. Questionnaires

2.3.1. The Korean version of the Neurological Disorders Depression Inventory for Epilepsy

The K-NDDI-E is a reliable and valid screening tool for the detection of major depression in Korean PWE.²³ This tool consists

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