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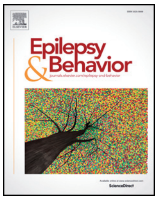

EQ-5D-based utilities and healthcare utilization in Thai adults with chronic epilepsy

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ABSTRACT

Quality of life and resource use are key parameters that justify economic values in treatments for epilepsy. Health profiles and service utilization were assessed in 224 adults with 15.7 years of epilepsy in two super-tertiary care facilities in Thailand. The European Quality of Life, 5-Dimension (EQ-5D)-based utilities and subsequent outpatient (OP) visits and hospitalizations were determined with respect to seizure control outcomes that were assessed by neurologists. Mean utility and visual analogue scale (VAS) scores were respectively higher in 67 patients who are seizure-free (0.82 and 78.9) than in 157 patients who had uncontrolled or persistent seizures, which were divided into seizure reduction (0.79 and 75.5) and no improvement in seizure frequency (0.72 and 73.5). Controlling for patient characteristics, those who are seizure-free had significantly higher utility and VAS scores than those with no improvement by 0.10 (95% confidence interval (CI): 0.03–0.17) and 6.25 (95% CI: 0.09–12.41), respectively. Seizure-free patients were less likely to report pain or discomfort, as compared with patients with seizure reduction (odds ratio (OR): 0.41, 95% CI: 0.19–0.90) and patients with no improvement (OR: 0.32, 95% CI: 0.13–0.75). Over a six-month period, mean OP visits were significantly lower in seizure-free patients (2.27 times) than in those with seizure reduction (3.00 times) and those with no improvement (4.08 times). Mean hospitalizations over 12 months among the three groups were 0.03, 0.24, and 0.14 times, respectively. For persistent seizures, 50% received only conventional antiepileptic drugs (AEDs). When epilepsy treatments are considered for their costs and effectiveness, utilities and healthcare use, conditional on seizure control status, can be applied for further analyses.

1. Introduction

Epilepsy is one of the most common chronic neurologic disorders, and its burden is extensive because of the unpredictable nature of disease, stigma, life-style restrictions, and side effects of seizure control medications [1–3]. These factors have negative effects on a patient's health status and quality of life and require increased use of health services. Studies have shown that quality of life in patients with epilepsy is lower than that in the general population and in patients with other chronic conditions [4,5]. Not all patients with epilepsy have their seizure completely controlled with antiepileptic drugs (AEDs). Uncontrolled or persistent seizures are particularly burdensome, requiring multiple medications, hospitalizations, and other medical services.

In Thailand, the prevalence of epilepsy was estimated to be 7.2 per 1000 adults based on a survey in rural areas [6]. Up to 30% of adults with epilepsy in this survey were found to have uncontrolled seizures, some reporting that they had disabling seizures. Both physical and psychological functions were diminished in patients with epilepsy [5]. Apart from anxiety and depression, seizure frequency was significantly associated with lower quality of life of Thai patients, as measured by the Quality of Life in Epilepsy Inventory (QOLIE-31) [7]. In a study of Malaysian patients, worry about seizures was the most influential predictor of quality of life as measured using the QOLIE-31 [8].

Although there are numerous studies about health-related quality of life of patients with epilepsy, few have been conducted in Southeast Asia and in developing countries where higher prevalence of epilepsy was reported [4,9]. Most studies on the patients' quality of life used

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Abbreviations: AEDs, antiepileptic drugs; EQ-5D, European Quality of Life, 5-Dimension; QOLIE, Quality of Life in Epilepsy Inventory; ILAE, International League Against Epilepsy; OP, outpatient; PNI, Prasat Neurological Institute; UCS, Universal Coverage Scheme; VAS, visual analogue scale; WHO, World Health Organization.

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disease-specific measures, such as QOLIE-31, QOLIE-89, Side Effects and Life Satisfaction Scale, and Washington Psychosocial Seizure Inventory, which cannot be converted into utility scores for further cross-disease comparison [5]. Most health technology assessment guidelines recommend European Quality of Life, 5-Dimension (EQ-5D) to assess patients' health profiles, and population-based algorithm to convert the health profiles into utility scores [10–12].

In Thailand, new generation AEDs have been available with a relatively higher price than conventional AEDs of which generic versions are available. Many patients with epilepsy require continuous medical treatments; therefore, long-term consequence on quality of life and health resource use should be assessed apart from clinical outcomes and costs of treatments. The objectives of this study were to determine utilities and subsequent healthcare utilization, conditional on seizure control status. Furthermore, utilization pattern of AEDs was examined.

2. Methods

2.1. Study design and patient selection

This is a cross-sectional study conducted at Srinagarind Hospital, the largest teaching hospital in the Northeastern Region, and at Prasat Neurological Institute (PNI), a specialized care facility in Bangkok, Thailand. The study was approved by the institutional review boards of these two hospitals. Both Srinagarind Hospital and PNI are public referral facilities, serving mostly patients who did not respond to conventional treatments.

The inclusion criteria for this study were adults (age ≥ 18 years) whose epilepsy had been diagnosed for at least two years and who had medical treatment for at least one year at the study sites. In addition, patients were to be seizure-free for at least one week before an interview. Patients with serious cognitive impairment or intellectual disability, with a stroke in the past three months, or having brain surgery were excluded. All participants were required to provide signed informed consent.

2.2. Questionnaire

A set of questionnaires was developed to collect data on patient sociodemographics, clinical aspects of epilepsy, health-related quality of life, use of health services, and use of specific AEDs. The clinical epilepsy consisted of seizure control outcomes and underlying covariates, including seizure type and causes, age at diagnosis, duration of epilepsy, family history of epilepsy, and history of febrile seizure.

Based on patient-recorded diaries of seizure frequency over a 12-month period, seizure control status was assessed by neurologists using the 2001 International League Against Epilepsy (ILAE) classification [13]. The seizure control was classified into three groups: (1) seizure-free or controlled seizure (class 1–2: completely seizure-free or only aura without seizure); (2) seizure reduction (class 3–4: 1–4 seizure days or ≥50% reduction in the number of seizure days); and (3) no improvement (class 5–6: <50% reduction in seizure days or increase in seizure days).

Seizure type was categorized based on the 1981 ILAE classification as follows: (1) partial seizure; (2) generalized seizure; and (3) unclassified seizure [14]. Seizure causes which were based on the 2010 ILAE Commission on Classification and Terminology included symptomatic, cryptogenic, and idiopathic epilepsy [15].

Patient's quality of life was assessed using European Quality of Life, 5-Dimension, 3-Level (EQ-5D-3L) questionnaire, a generic, preference-based instrument. At the time of the present study, the EQ-5D-3L version has been translated into Thai language and validated for psychometric properties in the general population [16]. The five dimensions, each representing perceived health problem with three (none, moderate, and severe) levels are (1) mobility, (2) self-care, (3) usual activities, (4) pain or discomfort, and (5) anxiety or depression. For an individual patient, responses to the five dimensions were converted into a single, preference-based index or utility via a formula that was derived from the time-trade-off approach in the Thai population as below [12,16].

$$\begin{aligned}\text{Utility} = 1-(&0.152 + 0.075M_2 + 0.418M_3 + 0.054S_2 + 0.102S_3 \\ &+ 0.044U_2 + 0.133U_3 + 0.08P_2 + 0.194P_3 + 0.063A_2 + 0.112A_3)\end{aligned}$$

where M is mobility, S is self-care, U is usual activities, P is pain/discomfort, and A is anxiety/depression and the subscript numerals represent the response level for each domain (e.g., $M_2 = 1$ if the patient has a moderate problem with mobility, 0 otherwise, and $M_3 = 1$ if the patient has a severe problem with mobility, 0 otherwise). The resulting utility score ranges from 0 for death to 1.0 for full health.

Apart from the descriptive EQ-5D, the questionnaire includes a visual analogue scale (EQ-VAS) of patients' self-rated health on the 20-cm vertical scale with a score range from 0 (the worst possible health status) to 100 (the best possible health status). The EQ-VAS provided complementary information on patients' summarizing views on their own health.

Use of health services associated with an occurrence of seizures was quantified in three categories: (1) outpatient (OP) visits to the study site in the last 6 months; (2) OP visits to other health care facilities in the last 6 months; and (3) admissions to any hospitals in the last 12 months. A relatively shorter recall period for the OP visits than that for hospitalization is consistent with that used in the national household survey in Thailand [17].

Use of AEDs was examined for distribution pattern in patients with persistent seizures and seizure-free patients. The AEDs were divided between conventional type and new generation. The conventional AEDs included phenobarbital, phenytoin, sodium valproate, and carbamazepine. New generation AEDs consisted of topiramate, lamotrigine, levetiracetam, oxcarbazepine, vigabatrin, zonisamide, gabapentin, and pregabalin. All AEDs, except for oxcarbazepine, zonisamide, and pregabalin, are included in the Thai National List of Essential Medicines. The proportion of patients receiving two or more AEDs with the doses greater than the World Health Organization (WHO)-defined daily doses was determined [18].

2.3. Data collection

Two data collectors were trained for use of the questionnaires. Quality assurance of data collection was observed in 20% of study patients by the research physicians using a protocol checklist. Data on the EQ-5D-based health profiles and use of health services were obtained using face-to-face interviews. The interview sessions lasted approximately 20 min on average. Other variables were extracted by chart review or patients' diaries.

2.4. Data analysis

Baseline characteristics of each seizure control group, including sociodemographics of patients (age, gender, residential area, education, employment, and health insurance), and clinical aspects of epilepsy were described and compared with each other using an analysis of variance (ANOVA) for continuous variables and chi-square statistics for categorical variables.

Utilities of subgroup of patients with partial seizure were compared visually with those calculated from EQ-5D-3L of the Thai general population and people having selected chronic diseases in Health and Welfare Survey (HWS), a cross-sectional survey of nationally representative households in 2011 [17].

Estimating the difference in utilities, health profiles, and health service utilization across the three seizure control groups was based on multivariable analysis that controlled for the same set of mentioned baseline characteristics. The utility and VAS scores for seizure reduction and no improvement were compared with those for the seizure-free