

## SEIZURE SEVERITY AS AN ALTERNATIVE MEASURE OF OUTCOME IN EPILEPSY

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### ABSTRACT

Seizure severity emerges as an important aspect of epilepsy. This is most relevant in refractory patients in whom complete remission of seizures is unlikely and reduced seizure severity may be a significant determinant of psychosocial well-being with a consequent improvement in quality of life (QOL). Thus a valid measure of seizure severity can serve both as an indicator of clinical outcome and as an evaluation tool of the interaction between seizures and the psychosocial complications of epilepsy.

After a brief review of the most frequently used scales measuring seizure severity in adults with epilepsy we have explored the relationship between seizure severity and QOL in a set of 103 patients. Two self-evaluation questionnaires were applied: the Seizure Severity Questionnaire (SSQ) and the Quality of Life in Epilepsy Inventory (QOLIE-31). The severity of the coexisting depression, an important confounder in the relationship between seizure severity and QOL, was assessed by the Hamilton Depression Rating Scale (HAMD-17).

All domains of the Quality-of-Life in Epilepsy Inventory (QOLIE-31) correlated highly significantly with seizure severity ( $p \leq 0.01$ ). The correlation was strong for the Overall score ( $r = -0.70$ ;  $p \leq 0.001$ ) and the Seizure worry domain ( $r = -0.71$ ;  $p \leq 0.001$ ). When the potentially confounding effect of depression was controlled for, the regression of seizure severity with the QOLIE-31 Overall score ( $P = 0.001$ ;  $R^2 = 0.56$ ) and the Seizure worry domain ( $P = 0.001$ ;  $R^2 = 0.50$ ) remained significant. These findings indicate that seizure severity is strongly associated with QOL in epilepsy and could be used as an alternative indicator of outcome in clinical research.

**Key words:** Seizure severity; Epilepsy; Quality of life; Seizure Severity Questionnaire;

### INTRODUCTION

Traditionally, outcome assessment in epilepsy has pertained mainly to seizure frequency. Clearly, there are more variables that may be relevant for the patients and determining seizure frequency as the only measure of efficacy suggests that potentially useful treatment effects are disregarded. This is most important in refractory patients in whom complete remission of seizures is unlikely and reduced seizure severity may be a significant determinant of psychosocial well-being with a consequent improvement in quality of life (QOL). As seizure severity encompasses two subdivisions—one relating to the manifestation of the seizures and their after-effects and the other relating to the patients' perception of control over the seizures, the pertinent question to be posed is how seizure severity should be measured: patient or observer? Moreover, in the absence of a standardized physical scale, are all measurements, observer or patient-based, not subjective? [1, 2]

Several scales have been developed to assess seizure severity in adults, both objectively, from the clinician's perspective (by assigning weights to various states to aspects of seizures) and subjectively, from the patient's perspective.

The VA (Veterans Administration) Seizure Frequency and Severity Scale (VA Scale) is a physician-based scale and relies on specific questions about seizure components performed by examination and interview [3]. Its construction is based on the frequency of the three types of partial-onset seizures and reflects the idea that the three most common seizure types in adults are not equally severe. After calculating a score based on the seizure type and frequency, the score is reduced by reviewing a series of modifying circumstances. In the opinion of Cramer and French, the VA scale does not meet the current standard for scale development [4].

The Chalfont Seizure Severity Scale is designed by

Duncan and Sander in 1991 as a measure of the seizure components that cause patients the most disturbances [5]. The scale is completed by the physician in an interview with the patient and an eye-witness of the seizures. Severity scores are provided for different seizure types and are modified by factor weightings representing a consensus view of patients, carers and professionals. A refined version of this scale is the National Hospital Seizure Severity Scale (NHS3) which is quicker and simpler to apply and measures seizure severity in a manner compatible with the subjective impression of people with epilepsy [6].

The Liverpool Seizure Severity Scale was developed to assess patient-perceived seizure severity [7]. It consists of two subscales: perception of control and ictal and postictal effects. The format of the scale does not provide information about the exact number of the seizures and the specific seizure classification has to be documented by an epileptologist [4]. The Liverpool Seizure Severity Scale has been included in a multidimensional model for QOL in epilepsy [8].

The Seizure Severity Questionnaire (SSQ) is designed as a self-reported assessment tool which categorizes seizures into three phases: warning, ictal activity and postictal recovery. The recovery phase is subdivided into three components as cognitive, emotional and physical aspects of recovery, each rated for frequency, severity and bothersomeness. Overall assessment of seizure severity is measured with the last two items [9]. Thus the SSQ appears as a multidimensional patient-reported assessment of seizure components, expanding inquiries into the recovery period as the most problematic aspect of seizures [10].

In an attempt to explore alternative measures of outcome in epilepsy, **the aim** of the present study was to evaluate relationships between seizure severity and specific aspects of QOL in adults with idiopathic epilepsy both assessed from patient-perceived point of view.

## METHODS

**A cross-cultural translation** of the SSQ into Bulgarian was conducted following international rules (translation, back-translation and cognitive debriefing in a group of five patients with epilepsy). Our goal was to achieve conceptual equivalence and cultural relevance of the translated items and ensure that the translated instrument was comprehensible to the Bulgarian patients [11]. The final version was tested in a pilot study including 10 patients who confirmed a high level of item acceptance. The layout and the images of the Bulgarian version were identical to the original instrument.

**Study population:** One hundred three outpatients were enrolled consecutively from an unselected patient population after presenting at their planned or spontaneous consultation. Eligible patients were those between the ages

of 18 and 60 with a proved diagnosis of idiopathic epilepsy for at least one year, with good knowledge of Bulgarian language and ability to read and write. The patients were excluded if they had significant comorbid medical illness, cranial trauma or craniotomy during the past year. Subjects with cognitive impairment or other serious psychiatric conditions were also excluded except for comorbid depression as defined by the ICD-10 criteria [12].

**Study design:** The study was conducted in two parts. In the first one the patients' eligibility was proved by a neurologist and two self-assessment instruments were administered: the SSQ and the Quality-of-Life in Epilepsy Inventory (QOLIE-31) [13]. The former has been already described. The latter-the QOLIE-31 questionnaire is a self-administered, widely used measure of QOL in epilepsy, derived from a longer disease-specific inventory, the QOLIE-89 [14]. It consists of 31 questions divided into seven domains: Seizure worry, Overall QOL, Emotional well-being, Energy/Fatigue, Cognitive functioning, Medication effects and Social functioning, as well as an overall score. The responses can yield individual scores (per subscales) and a total (composite) score. Higher scores indicate better QOL with values ranging from 1 to 100. Question 31 is a subjective assessment of one's general health condition and is not included in the total QOL score. A validated Bulgarian version of the QOLIE-31 has been used [15].

In the second part of the study the patients were evaluated for coexisting depression by a psychiatrist. The Hamilton Depression Rating Scale (HAMD-17) was used to assess its severity [16]. The HAMD-17 is originally constructed as an interviewer-rated instrument for evaluation of the severity of depression. It is a 17 item questionnaire exploring 10 domains associated with depression: mood, anxiety, sexual function, appetite, sleep, functional status, physical symptoms, hypochondriasis, diurnal variation, general psychiatric distress. To quantify symptom severity, for each item, a score is devised ranging from 0 (normal) to 2 or 4 (maximal impairment). Based on the HAMD-17 scores, depression was defined as mild (8-17 points), moderate (18-24 points) and severe ( $\geq 25$  points).

**Statistical analysis:** Statistical analyses were Spearman's correlations for univariate analyses and multivariate linear regression for assessing the independent effect of seizure severity on QOL domains after controlling for mood scores. All P values were two-sided with statistical significance evaluated at the  $\alpha=0.05$  level. The beta value was used as a measure of how strongly each predictor variable influences the criterion variable. The adjusted RI was used to assess the rate of variance of the domain score explained by the full model. Ninety-five percent confidence intervals (95% CI) were calculated to assess the precision of the  $\beta$  values obtained. Data processing and analysis were carried out using SPSS for Windows (Version 17.0; SPSS Inc., Chicago, IL).

## RESULTS

One hundred three eligible patients, of which 41 (39.8%) were males and 62 (60.2%) were females, with a mean age of 37.1 (SD:  $\pm 11.6$ ), were enrolled consecutively into the study.

All domains of the Quality of Life in Epilepsy-31 (QOLIE-31) correlated highly significantly with seizure severity ( $p \leq 0.01$ ) as did the Overall score (Table 1). The correlation was strong for the Overall score ( $r = -0.70$ ;  $p \leq 0.001$ ) and the Seizure worry domain ( $r = -0.71$ ;  $p \leq 0.001$ ) and moderate for all other domains but the Medication effects. When the potentially confounding effect of depression, measured by HAMD-17, was controlled for, the regression of Seizure severity with the QOLIE-31 Overall score ( $P = 0.001$ ;  $R^2 = 0.56$ ) and the Seizure worry domain ( $P = 0.001$ ;  $R^2 = 0.50$ ) remained significant (Table 2).

## DISCUSSION

The aim of the present study was to evaluate the relationship between two self-report measures of seizure severity and QOL in adults with idiopathic epilepsy.

Quality of life is a multidimensional concept, acknowledged as an important outcome measure in epilepsy. It incorporates physical, psychological, social and economic domains. It is recognized that QOL assessment should come primarily from the patient, with ancillary material provided by family and health care providers. The balance between perceived and desired status is the essence of the QOL [17]. The assessment of disease severity is another controversial issue in epilepsy. As highlighted by Cramer, the major problems inherent in assessing seizure severity are dependence on patient recall and reporting, and observer documentation [17]. Various scales have been developed to assess seizure severity both objectively from the clinician's perspective on the various aspects of the seizures and subjectively, from the patient's perspective. In parallel, the development of QOL measures using subjective patient-based opinion has changed the approach to seizure severity assessment [18]. As already mentioned, most of the scales reflect patients' as well as physician's opinion and sharp division between "patient-based" and "physician based" scale is inappropriate [1]. SSQ has been developed as a multidimensional patient-reported assessment of seizure components. Based on comments from patients and

families that the recovery period was the most problematic aspect of seizures, the SSQ expanded inquiries into recovery from cognitive, emotional, and physical effects of seizures [10].

Mood disturbance is a key factor in patients' judgment of their QOL. Patients with epilepsy have a high psychiatric morbidity with prevalent anxiety and mood disorders. Evaluating the relationship between depressive symptoms and seizure severity Sancho et al. found that clinically depressed people with epilepsy reported higher levels of all aspects of seizure severity, as well as increased difficulties with overall seizure recovery, when compared with non-depressed controls with epilepsy [18]. The findings of Cramer et al. further emphasized the strong correlation between seizure severity and depression [10]. Because anxiety and depression are associated with significantly poorer QOL, it is important to reduce seizure severity, anxiety and depression, and improve QOL of the patients [19]. Our results provide evidence that there is an association between seizure severity and quality of life, even when controlling for such an important confounder as depression. As Harden et al. suggest, seizure severity may promote the development or exacerbation of worry and anxiety in epilepsy [20]. Seizure worry, as measured by the QOLIE-31, consists of such items as worry about future seizures, apprehension over future injury resulting from seizures, trepidation over adverse side effects of medication regimens, and social embarrassment over having seizures. Anxiety itself has an important effect on QOL in epilepsy. In a study conducted by Cramer et al. it was reported that being a strong predictor of QOL, anxiety contributed to one-third of the variance in scores [21].

In conclusion the reported findings suggest that reducing seizure severity improves the QOL of the patients with epilepsy. Identifying and treating anxiety and depression among these patients is of great importance for improving their seizure severity perception and QOL. The perfect assessment of outcome in epilepsy should be a combination of well validated and reliable measures pertaining to specific physical and psychosocial aspects of QOL with medical-professional outcome variables in epilepsy. We agree that the final proof of their usefulness must come from clinical trials [1].

**Table 1.** Correlation between seizure severity and QOLIE-31 domains (N = 103)

QOLIE-31 domain	Spearman's correlation coefficient	P value
Overall score	-0.7	≤ 0.001
Seizure worry	-0.71	≤ 0.001
Overall quality of life	-0.6	≤ 0.001
Emotional well-being	-0.53	≤ 0.001
Energy/Fatigue	-0.55	≤ 0.001
Cognitive functioning	-0.48	≤ 0.001
Medication effects	-0.25	≤ 0.01
Social functioning	-0.62	≤ 0.001

**Table 2.** Multivariate linear regression (controlling for mood scores) between seizure severity and QOLIE-31 domains (N = 103)

QOLIE-31 domain	P value	R <sup>2</sup> value	β value	95% CI
Overall score	0.001	0.56	-0.469	-0.299 to 0.203
Seizure worry	0.027	0.5	-0.393	-0.047 to -0.003
Overall quality of life	0.767	-	-0.063	-0.049 to 0.036
Emotional well-being	0.605	-	0.113	-0.034 to 0.059
Energy/Fatigue	0.477	-	-0.124	-0.046 to 0.022
Cognitive functioning	0.706	-	0.158	-0.056 to 0.082
Medication effects	0.744	-	0.034	-0.010 to 0.014
Social functioning	0.967	-	-0.018	-0.056 to 0.054

R<sup>2</sup> value - R-squared value

β value - regression coefficient

CI - Confidence Intervals

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