

Seizure frequency and severity: How really important are they for the quality of life of patients with refractory epilepsy

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Abstract

Introduction: The data in the scientific literature about the significance of seizure severity and frequency for the quality of life (QOL) of patients with refractory epilepsy (RE) are contradictory. **Objective:** Our objective was to assess the impact of the seizure severity and frequency on the QOL of Bulgarian patients with RE. **Materials and Methods:** A total of 70 patients with RE were studied by examining the medical documentation and seizure diaries. All study participants completed quality of life epilepsy inventory (QOLIE-89). Seizure severity of only 59 patients who had a seizure in the last month was assessed by the Liverpool seizure severity scale. **Results:** A limited negative impact of the seizure severity and frequency on some aspects of the physical health, epilepsy, all aspects of the social health and epilepsy and the overall QOL has been demonstrated. A weak to moderate reverse correlation between the specified factors and the respective QOLIE-89 subscales has been found. **Conclusion:** The clinical factors seizure severity and seizure frequency have a limited negative impact mostly on the social aspects of QOL. The study results support the multidisciplinary approach to persons with epilepsy.

Key Words

Frequency, quality of life, refractory epilepsy, seizure, severity

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Introduction

The quality of life (QOL) of people with epilepsy is lower than that of the general population and of people with other chronic diseases. Epilepsy has an enormous influence on all three levels of the QOL (physical, mental and social health), which is exercised directly-by impairing the physical and mental health and indirectly – by introducing limitations and decreasing opportunities for participation in QOL improving activities. The explanation of these phenomena is the presence of clinical insecurity. It has been proven that the QOL of patients with epilepsy is comparable with that of healthy people in cases with a satisfactory seizure control and lower in cases with a higher seizure frequency.^[1] A variety of clinical, psychological, social and demographic factors have influence over the QOL. Harden *et al.* have demonstrated that the seizure severity correlates with

the seizure worries and the social functioning. In some cases, the influence is indirect – by increasing the depressive symptoms, anxiety and the behavior of social avoidance.^[2] A lot of scientists have confirmed the moderate to very significant role of the seizure frequency and severity (especially in cases with more than 1 seizure/month) over QOL in patients with epilepsy.^[3-7] Tracy *et al.* have found that the seizure control is associated with the overall score of QOL and some quality of life epilepsy inventory (QOLIE-31) subscales – “seizure worry” and “social function”.^[8] According to Van Hout *et al.* (1997) the seizure control correlates with other QOL aspects – everyday activities, mental health, health perceptions and social life.^[9] Råty and Wilde Larsson *et al.* have proven the negative correlation of the high seizure frequency with the QOL aspects general health and mental/spiritual sphere.^[10] Tlusta *et al.*,^[11] Sachin *et al.*,^[12] and Gromov *et al.*^[3] have demonstrated a significant association of all QOL aspects with the seizure frequency. Mrabet *et al.* have discovered that the QOL correlates with the seizure frequency, the time from the last seizure and the adverse effects from antiepileptic drugs.^[13] Some investigators have concluded that only the complete seizure control is associated with a QOL improvement.^[1,14]

Objective

Our purpose of this study was to assess the impact of the seizure frequency and severity on the of Bulgarian patients with refractory epilepsy (RE).

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Materials and Methods

The study was performed with the participation of a representative selection of 176 consecutive patients with RE who attended the Clinic of Neurology at the University Hospital in Plovdiv, Bulgaria for a regular examination or in cases of unsatisfactory seizure control or adverse events from treatment and fulfilled the study inclusion criteria.

All study procedures were performed after the approval of the Local Ethics Commission at the University of Medicine, Plovdiv. Every patient was introduced to the study design and signed an informed consent form before participating in the study procedures.

The following inclusion criteria were used: age between 18 and 65 years; a diagnosis of RE; lack of cognitive impairment based on evaluation rapide des fonctions cognitives (Gil, 2006) with a score <47 in patients up to 60 years of age and primary education or <46 in patients between 60 and 65 years of age and less than a primary education or illiterate;^[15] lack of progressive somatic or neurological disease; lack of a simple or complex partial seizure in the last 4 h; and lack of generalized tonic-clonic seizure in the last 24 h; a signed informed consent form. Epilepsy was defined as refractory when adequate seizure control had not been achieved with at least two appropriately selected anti-epileptic drugs prescribed as mono- or polytherapy at maximally tolerated doses for a period of at least 2 years. After excluding 39 patients with pseudo-RE (in cases with diagnostic, therapeutic errors or poor compliance), 2 patients older than 65 years, 2 patients with progressive neurological disease, 5 patients with a simple or complex partial seizure in the last 4 h or a generalized tonic-clonic seizure in the last 24 h and 58 patients with cognitive impairment, 70 patients with RE were included in the study. Both groups were similar with respect to age and gender. The response rate for the study (the percentage of patients who fulfilled the inclusion criteria) was 39.77%.

The data were collected by a trained health professional using a purposeful interview on the patients' disease course, as well as by examining the patients' medical documentation and seizure diaries. All study participants completed QOLIE-89. The Liverpool seizure severity scale (LSSS) was completed by 59 patients with RE. The rest of the study participants did not complete this scale because they had not had a seizure in the previous month and their seizure severity was not assessed. The LSSS is a self-assessment scale, which is used to determine the seizure severity by means of the patient's subjective assessment of the most severe seizure during the last month. The total number of questions is 20 and they are divided into 2 subscales: Perceptive subscale (8 questions about seizure severity and the seizure control perception) and ictal/postictal subscale (12 questions about the preictal, ictal and postictal characteristics). The assessment of every statement varies between "0" and "4" depending upon the extent to which the respective seizure aspect is perceived as a problem by the patient.^[16] It has been translated into Bulgarian by a trained translator and some specifications were made after a consultation with a neurologist specialized in epilepsy. QOLIE-89 is the most understandable and the most widely used instrument for QOL assessment in

patients with epilepsy. Its items are distributed in 17 subscales, which characterize 4 basic factors directed toward epilepsy, physical, mental and social health. The overall score QOLIE-89 is calculated in several stages. The so-called "T-scores" for each of the 17 subscale final scores and for the overall score are often used. They represent linear transformations of the scores that produce a mean of 50 and standard deviation of 10 for a cohort of 304 adults with epilepsy. Higher T-scores reflect a more favorable QOL. In the course of the study, a validation of the Bulgarian translation of QOLIE-89 was made and its reliability and internal consistency were demonstrated.^[17]

The collected primary information was checked, encoded and entered into a computer database for statistical analysis. The data were processed using STATA Version 10 (Stata Corp., College Station, TX, U.S.A.) and SPSS (Statistical Package for the Social Sciences), version 14.0 (SPSS Inc., Chicago, IL, U.S.A.). The results for quantitative variables were expressed as \bar{x} (the mean) \pm SE (standard error). The results for qualitative variables were expressed as percentages. Pearson's correlation coefficient (r_{xy}), χ^2 test and Fisher criterion (F) were used to analyze the correlation between the seizure frequency, seizure severity, epilepsy duration, seizure type, type of epilepsy, number of antiepileptic drugs and assessments of the subscales and the overall score of QOLIE-89. Regression analysis was applied to estimate the simultaneous impact of seizure frequency and seizure severity on all aspects of QOL. Chi-square test was used to assess the association of seizure frequency with other categorical variables.

Results

Overall, 21 (30.00% \pm 5.48) of the study participants were men; the remaining 49 (70.00% \pm 5.48) were women. The mean age of patients was 41.72 \pm 1.08 years. Most of the participants (76.6%) were between 30 and 60 years of age. The mean disease duration was 25.07 \pm 1.32 years. The clinical findings of the study participants are presented in Table 1.

From the mentioned categorical variables, seizure frequency was associated only with epilepsy etiology [Table 2]. Patients with cryptogenic and symptomatic etiology had more frequent seizures when compared to idiopathic epilepsy syndromes.

The mean overall score of QOLIE-89, given by patients with RE, was 64.30 \pm 17.06. In our data analysis, the T-scores were used for a more explicit comparison with the mean scores of the epileptic population. The obtained scores were accepted as very low (≤ 35), low (36-45), medium (46-55) and high (> 55). As a T-score, the mean overall score of QOLIE-89 was a bit lower than the mean for the epileptic population (\bar{x} = 47.80). Low mean scores were obtained for the subscales "health perceptions" (\bar{x} = 39.43), "sexual relations" (\bar{x} = 42.50) and "overall QOL" (\bar{x} = 42.79). The mean scores of all other subscales were close to the mean for the epileptic population.

It was found that the duration of epilepsy had influence only on the subscale "change in health" $P < 0.05$ (χ^2 = 14.17). The greater duration is associated with health worsening during the last year, probably because of the accumulation of more concomitant diseases.

An impact of the type of epilepsy on the assessments of the subscale "seizure worry" was demonstrated $P < 0.05$ ($\chi^2 = 9.48$). Approximately, 50% of patients with partial epilepsy and the same percentage of those with generalized epilepsy gave low scores for this subscale, i.e., they had lots of worries about seizures. Nearly 27.7% of the participants having partial epilepsy and 5% of those having generalized epilepsy gave medium scores. High scores were given more frequently by the patients having generalized epilepsy (45%) compared to the ones with partial epilepsy (24.6%). An influence of the type of epilepsy on the overall score of QOLIE-89 was proven as well $P < 0.05$ ($\chi^2 = 9.67$). As a whole

the overall score of QOLIE-89 was lower in patients having partial epilepsy.

The seizure type had an impact on the subscale "overall health" $P < 0.05$ ($\chi^2 = 26.06$). All participants having simple partial seizures gave high scores for this subscale. The lowest scores were given by the patients having partial seizures with secondary generalization –55% gave very low and low scores, 30% – medium scores, 15% gave high scores. The greatest percentage of high scores (40.91%) were given by the participants having generalized tonic-clonic seizures and generalized myoclonic seizures, but the percentage of very low and low scores in this group was also high (40.91%). Of patients with polymorphic seizures 40.43% gave high scores, 25.53% – very low and low scores. 25% of the patients having complex partial seizures gave low scores, 50% – medium scores and 25% – high scores.

The number of antiepileptic drugs applied recently as mono- or polytherapy had an impact on the assessments of the subscale "overall health" $P < 0.05$ ($\chi^2 = 8.53$). An interesting result is the more frequent high scores given by the patients on polytherapy, $P < 0.01$ ($r_{xy} = 0.22$).

The seizure frequency and seizure severity are important clinical factors the influence of which is investigated. The impact of seizure severity on most aspects of the QOL is demonstrated in Table 3.

A significant difference between the scores of some QOLIE-89 subscales ("change in health," "work/driving/social function," "social support," social isolation," "overall QOL") given by patients having seizures with different severity (according to LSSS) was proven. A moderate reverse correlation was found for these subscales. The conclusion that the social aspects of QOL and the overall QOL are worse in cases with greater seizure severity is drawn. Etiology was found to be the only co-factor of seizure severity for the subscale "social isolation" scores ($F = 6.25$, $P < 0.01$).

The seizure frequency has an impact on some aspects of the QOL as well – Table 4. A significant difference between the scores of some QOLIE-89 subscales ("social support," social isolation," "seizure worry," "medication effects," "overall health") given by patients having seizures with different frequency was proven. A weak to moderate reverse correlation was found for these subscales. The conclusion that the social aspects of QOL, the worries about seizures and adverse events from medications and the overall health are worse in cases

Table 1: Clinical findings of the study participants

Clinical finding	N	P (%)	SE
Type of epilepsy			
Partial	53	75.71	5.11
Generalized	16	22.86	5.03
Not defined	1	1.43	–
Etiology of epilepsy			
Idiopathic	17	24.29	5.13
Symptomatic	28	40.00	5.86
Cryptogenic	25	35.71	5.73
Type of seizures			
Partial			
Simple partial	1	1.43	–
Complex partial	1	1.43	–
Partial with secondary generalization	15	21.43	4.87
Generalized			
Generalized tonic-clonic	15	21.43	4.87
Generalized myoclonic	1	1.43	–
Polymorphic	37	52.86	5.97
Recent seizure frequency			
1/several years	2	2.86	–
1-11 seizures/year	11	15.71	4.35
1-3 seizures/month	21	30.00	5.48
1-6 seizures/week	32	45.71	5.95
Daily seizures	4	5.71	–
Seizure severity (LSSS score)			
Mild (1-20)	8	13.56	2.14
Moderate (21-40)	32	54.24	6.22
Severe (41-60)	18	30.51	4.31
Very severe (61-80)	1	1.69	–
Therapy			
Monotherapy	7	10	3.59
Polytherapy	63	90	3.59

SE = Standard error, LSSS = Liverpool seizure severity scale

Table 2: Association of the seizure frequency with epilepsy etiology

Etiology	Seizure frequency			Total N (P %)
	1-11 seizures/year N (P %)	1-3 seizures/month N (P %)	1-6 seizures/week N (P %)	
Idiopathic	4 (23.5)	9 (52.9)	4 (23.5)	17 (100.0)
Cryptogenic	1 (4.0)	8 (32.0)	16 (64.0)	25 (100.0)
Symptomatic	8 (28.6)	4 (14.3)	16 (57.1)	28 (100.0)
Total	13 (18.6)	21 (30.0)	36 (51.4)	70 (100.0)

Chi-square tests. Pearson Chi-square 13.430, df 4, Asymp. Significant (2-sided) $P < 0.05$. Likelihood ratio 15.150, df 4, Asymp. Significant (2-sided) $P < 0.05$. Linear-by-linear association 15.292, df 1, Asymp. Significant (2-sided) $P = 0.390$

Table 3: Impact of the seizure severity on different aspects of the QOL

QOLIE-89 subscale	LSSS score	\bar{x}	SE	F	-	r_{xy}
Health perceptions	1-20	43.34	5.96	0.98	>0.05	-
	21-40	38.85	1.99			
	≥41	36.37	2.41			
Physical function	1-20	53.65	3.13	0.97	>0.05	-
	21-40	50.71	1.57			
	≥41	48.40	2.24			
Role limitations-physical	1-20	55.70	2.90	1.41	>0.05	-
	21-40	49.90	1.85			
	≥41	47.74	2.17			
Pain	1-20	53.30	3.30	1.12	>0.05	-
	21-40	49.77	1.76			
	≥41	46.68	2.95			
Energy/fatigue	1-20	51.53	4.72	1.96	>0.05	-
	21-40	48.04	1.44			
	≥41	44.15	2.22			
Health discouragement	1-20	51.85	2.55	2.47	>0.05	-
	21-40	46.69	1.56			
	≥41	43.25	2.50			
Change in health	1-20	71.88	5.66	4.44	<0.05	-0.34
	21-40	52.34	3.43			
	≥41	46.05	5.50			
Sexual relations	1-20	50.00	10.56	0.51	>0.05	-
	21-40	42.97	5.64			
	≥41	36.84	7.49			
Role limitations-emotional	1-20	53.10	3.95	0.82	>0.05	-
	21-40	53.10	1.72			
	≥41	49.14	3.00			
Emotional well-being	1-20	49.90	3.06	2.96	>0.05	-
	21-40	48.03	1.63			
	≥41	41.32	3.04			
Attention/concentration	1-20	53.00	2.21	1.44	>0.05	-
	21-40	46.82	1.80			
	≥41	46.50	2.40			
Memory	1-20	59.28	3.49	2.51	>0.05	-
	21-40	51.94	1.80			
	≥41	49.15	2.74			
Language	1-20	56.88	2.52	0.40	>0.05	-
	21-40	53.45	1.98			
	≥41	52.88	2.68			
Work/driving/social function	1-20	53.68	3.03	4.09	<0.05	-0.36
	21-40	48.36	1.33			
	≥41	43.77	2.28			
Social support	1-20	57.59	3.42	3.94	<0.05	-0.34
	21-40	55.04	1.49			
	≥41	47.82	2.92			
Social isolation	1-20	54.28	3.98	3.26	<0.05	-0.31
	21-40	51.72	1.84			
	≥41	44.19	3.09			
Seizure worry	1-20	49.34	4.63	1.65	>0.05	-
	21-40	44.64	1.71			
	≥41	41.49	2.38			
Medication effects	1-20	57.34	4.07	2.62	>0.05	-
	21-40	50.65	1.65			
	≥41	47.38	2.63			

(Continued)

Table 3: (Continued)

QOLIE-89 subscale	LSSS score	\bar{x}	SE	F	-	r_{xy}
Overall health	1-20	43.13	8.91	1.89	>0.05	-
	21-40	54.84	3.40			
	≥41	45.52	4.31			
Overall QOL	1-20	49.96	2.51	4.70	<0.05	-0.38
	21-40	42.54	1.70			
	≥41	37.49	2.51			
Overall score of QOLIE-89	1-20	52.57	2.71	2.59	>0.05	-
	21-40	47.84	1.79			
	≥41	42.67	3.04			

QOL = Quality of life, QOLIE = Quality of life in epilepsy inventory, SE = Standard error, LSSS = Liverpool seizure severity scale

Table 4: Impact of the seizure frequency on different aspects of the QOL

QOLIE-89 subscale	Seizure frequency	\bar{x}	SE	F	P	r_{xy}
Health perceptions	1-11/year	44.02	2.88	1.74	>0.05	-
	1-3/month	36.33	2.45			
	1-6/week	39.57	2.07			
Physical function	1-11/year	50.45	3.34	0.49	>0.05	-
	1-3/month	51.79	1.96			
	1-6/week	49.14	1.56			
Role limitations-physical	1-11/year	5.30	3.20	0.29	>0.05	-
	1-3/month	51.05	2.73			
	1-6/week	49.02	1.82			
Pain	1-11/year	50.95	2.71	0.22	>0.05	-
	1-3/month	49.28	2.35			
	1-6/week	48.65	1.86			
Energy/fatigue	1-11/year	50.30	2.45	0.66	>0.05	-
	1-3/month	46.46	2.16			
	1-6/week	47.48	1.61			
Health discouragement	1-11/year	51.02	2.13	1.38	>0.05	-
	1-3/month	47.20	2.27			
	1-6/week	45.91	1.59			
Change in health	1-11/year	59.62	4.51	0.99	>0.05	-
	1-3/month	55.95	3.82			
	1-6/week	50.69	4.04			
Sexual relations	1-11/year	42.31	7.69	0.68	>0.05	-
	1-3/month	48.81	6.79			
	1-6/week	38.89	5.31			
Role limitations-emotional	1-11/year	51.80	3.27	0.42	>0.05	-
	1-3/month	49.79	2.81			
	1-6/week	52.62	1.69			
Emotional well-being	1-11/year	48.82	2.28	0.58	>0.05	-
	1-3/month	47.03	2.15			
	1-6/week	45.24	1.96			
Attention/ concentration	1-11/year	52.60	2.83	2.63	>0.05	-
	1-3/month	49.86	2.36			
	1-6/week	45.78	1.54			
Memory	1-11/year	56.21	3.20	1.39	>0.05	-
	1-3/month	54.06	2.42			
	1-6/week	50.77	1.77			
Language	1-11/year	58.01	1.76	1.82	>0.05	-
	1-3/month	55.67	2.38			
	1-6/week	52.18	1.81			
Work/driving/social function	1-11/year	52.40	2.89	1.61	>0.05	-
	1-3/month	48.41	2.33			
	1-6/week	46.95	1.36			

(Continued)

Table 4: (Continued)

QOLIE-89 subscale	Seizure frequency	\bar{x}	SE	F	P	r_{xy}
Social support	1-11/year	55.30	2.93	3.08	<0.05	-0.23
	1-3/month	56.96	1.92			
	1-6/week	50.29	1.84			
Social isolation	1-11/year	54.66	2.11	3.92	<0.05	-0.30
	1-3/month	53.76	2.38			
	1-6/week	46.71	2.03			
Seizure worry	1-11/year	53.16	3.23	4.05	<0.05	-0.30
	1-3/month	45.03	2.56			
	1-6/week	43.33	1.64			
Medication effects	1-11/year	57.91	2.25	3.06	<0.05	-0.23
	1-3/month	50.00	2.12			
	1-6/week	50.24	1.85			
Overall health	1-11/year	65.38	4.62	3.18	<0.05	-0.24
	1-3/month	49.76	4.56			
	1-6/week	50.00	3.41			
Overall QOL	1-11/year	47.98	2.49	2.06	>0.05	-
	1-3/month	41.87	1.93			
	1-6/week	41.45	1.89			
Overall score of QOLIE-89	1-11/year	52.62	2.98	1.45	>0.05	-
	1-3/month	47.11	2.82			
	1-6/week	46.46	1.78			

QOL = Quality of life, QOLIE = Quality of life in epilepsy inventory, SE = Standard error

with higher seizure frequency is drawn. Therapy (mono- or polytherapy) was found to be the only co-factor of seizure frequency for the subscale "overall health" scores ($F = 4.53$, $P < 0.01$). Patients on monotherapy were more likely to have poorer scores on overall health subscale.

By means of a multivariate analysis, an impact of both seizure frequency and seizure severity on "medication effects" $F = 4.94$ ($P < 0.05$), "social support" $F = 6.4$ ($P < 0.01$) and "social isolation" $F = 5.34$ ($P < 0.01$) was proven.

Discussion

The objective of our study was to assess the impact of the seizure frequency and severity on the QOL of Bulgarian patients with RE. According to our study results, greater seizure severity was found to be associated with a negative change in health over the last year, poor work/driving/social functions, perception of poor social support and feeling of social isolation and poor overall QOL. Patients specified health perceptions, sexual relations and overall QOL as the most affected by RE aspects of QOL. Therefore, the great seizure severity has a negative impact on some aspects of the physical health, all aspects of the social health and the overall QOL and the increase in seizure severity is associated with a decrease in the respective aspects of QOL.

Etiology was the only co-factor of seizure severity for the subscale "social isolation" scores. Therefore, seizure severity could be accepted as an independent determinant of QOL. The seizure severity and its correlation with the QOL have been assessed by few scientists.^[18] The results from their studies support some conclusions from our investigation. Vickrey *et al.* (2000) and Zhao *et al.* have confirmed that the seizure severity correlates with the overall score of QOLIE-89 ($r = -0.424$,

$P < 0.01$).^[19,20] In the study of Todorova, the seizure severity accounted most for the QOLIE-31 subscale "seizure worry" (27.04%).^[21] Harden *et al.* have also found that the seizure severity is associated with scores of the QOLIE-31 subscales: "social functioning" ($r = -0.280$, $P = 0.002$) and "overall QOL" ($r = -0.210$, $P = 0.023$) but in contrast to our results they have proved a correlation of the seizure severity with the subscales "seizure worry" ($r = -0.265$, $P = 0.004$) and "cognitive function" ($r = -0.209$, $P = 0.024$).^[2] A possible explanation for some dissimilarities of study results is the usage of different seizure severity and QOL questionnaires.

Patients with great seizure frequency also specified health perceptions, sexual relations and overall QOL as the most affected by RE aspects of QOL. The high seizure frequency has a negative impact on most social aspects, some aspects associated with epilepsy and the overall health and the increase in seizure frequency is associated with a decrease in the respective aspects of QOL. Therapy (mono- or polytherapy) was the only co-factor of seizure frequency for the subscale "overall health" scores. Special features of Bulgarian mentality (to feel safer when on polytherapy) are a possible explanation about the poorer results of patients on monotherapy. Therefore, seizure frequency could be accepted as an independent determinant of QOL.

The seizure frequency is among the factors with the most frequently studied the impact on the QOL. Lots of investigators have supported the statement that the higher seizure frequency has a negative influence on the QOL.^[4,5,7-8,10,12,16,17,22-24] In the scientific literature, there is no agreement whether the clinical factors (seizure frequency most often cited) or the psychic factors (depression most often cited) are the main predictors of the QOL of people with epilepsy. Some investigators

have accepted the seizure frequency as a very significant QOL predictor. Djibuti *et al.* (2003) have proven its impact on the QOLIE-31 subscales "seizure worry," "overall QOL," "emotional well-being," "energy/fatigue," "cognitive function" and "social function."^[25] Guekht *et al.* (2007) have found a significant but rather weak correlation with all QOLIE-31 subscales and have confirmed that seizure frequency is the most significant parameter related to QOL ($r = 0.46$ with total score). Gromov *et al.*, Gusev *et al.* and Elsharkawy *et al.* have demonstrated that the achievement of a complete seizure control is associated with an improvement of all QOL aspects with the exception of cognitive functions and this effect remains relatively stable.^[3,14,26,27] Other scientists have obtained results similar to ours and have proven a low and/or partial influence on some QOL aspects.^[28] Velizarova-Stoimenova has found that the seizure frequency correlates with the level of satisfaction, the subjective assessment of cognitive functions, anxiety and fatigue.^[29] Todorova has demonstrated that the seizure frequency influences most the QOLIE-31 subscale "medication effects" (6.76%) and "social functioning" (36%).^[21] According to the study results of Tracy *et al.* the seizure control has a weak correlation with the overall score of QOLIE-31 and the scores of the subscales "seizure worry," "medication effects," "social function," and "overall QOL."^[8] Canuet *et al.* have confirmed that the seizure frequency is associated with variations of three QOLIE-31 subscales — "seizure worry," "cognitive function," "social function," but its impact is 3 times lower compared with depression.^[30] Senol *et al.* have determined the seizure frequency, depression and fatigue as the most significant factors for the assessments of the QOLIE-89 subscale "overall QOL," the Mental health domain and the directed to epilepsy subscales ($P < 0.001$).^[6] Zhao *et al.* have found a negative correlation of the seizure frequency with the overall score of QOLIE-89 ($r = -0.274$, $P < 0.01$).^[20] In contrast to these scientists Gilliam has not found a correlation between the seizure frequency and the subscales of QOLIE-89.^[31] A possible explanation for dissimilarities of various study results is the different study design, inclusion criteria and QOL questionnaires.

Limitations

The first limitation of our study is that only patients with RE completed QOLIE-89. Another limitation is that the results of this study can be applied only to the RE patients attending the university clinic and may not be generalized to the general population. However, these limitations do not devalue the results from our study. Further investigations of patients, having a variety of demographic, clinical and social characteristics, are needed.

Conclusion

The results from our study have shown that the seizure severity and the seizure frequency have a limited impact, mostly on the social aspects of QOL. These conclusions support the multidisciplinary approach to persons with epilepsy in Bulgaria with the participation of a neurologist, a specialist in epilepsy, psychologist, psychiatrist and a social worker, with the objective of making a more comprehensive estimation of patients' problems and reducing the negative influence of greater seizure frequency and severity.

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