IMPORTANCE OF SOME CLINICAL FACTORS (EPILEPSY DURATION, CLUSTERS OF SEIZURES AND/OR EPILEPTIC STATUS, TYPE OF EPILEPSY, TYPE OF SEIZURES, MONO-/ POLYTHERAPY) FOR THE QUALITY OF LIFE OF PATIENTS WITH REFRACTORY EPILEPSY

E. Viteva

Department of Neurology, Medical University of Plovdiv

Summary. To assess the impact of the duration of epilepsy, the clusters of seizures and/or epileptic status, the type of epilepsy and seizures, and the mono-/ polytherapy on the quality of life (QOL) of Bulgarian patients with refractory epilepsy (RE). Seventy patients with RE were studied using a purposeful interview on the patients' disease course, as well as an exam of the patients' medical documentation. All study participants completed QOLIE-89. The greater duration of epilepsy has a negative impact on the assessments of the change in health during the last year. Seizure clusters and/or epileptic status in the disease course are associated with lower assessments of the sexual relations. The type of epilepsy has an impact on: 1. Seizure worries – participants with generalized epilepsy have less worries; 2. The overall score of QOLIE-89 – the patients with partial epilepsy make lower assessments. An impact of the seizure type on the subscale "Overall health" has been demonstrated. The lowest scores are given by the patients having partial seizures with secondary generalization. The highest scores are given by the participants having generalized tonic-clonic seizures, generalized myoclonic seizures, and polymorphic seizures. The prescribed treatment as mono-/polytherapy has an impact on the assessments of the overall health – the scores were higher in cases with polytherapy. The clinical factors duration of epilepsy, clusters of seizures and/ or epileptic status, type of epilepsy, type of seizures, mono-/polytherapy have an impact on single aspects of the QOL of the patients with RE.

Key words: *quality of life, refractory epilepsy, duration, mono-/polytherapy, seizure clusters, epileptic status*

INTRODUCTION

Epilepsy has a great influence on the three levels (physical, mental and social health) of the quality of life of patients. A number of studies have demonstrated the impact of the patents' clinical, mental, social and demographic characteristics on their quality of life (QOL). Some of the clinical characteristics (epilepsy duration, clusters of seizures and/or epileptic status, type of epilepsy, type of seizures, mono-/polytherapy) have not been mentioned frequently in literature as QOL predictors. Piperidou et al. (2008) have proven that QOL is associated with the duration of epilepsy and the usage of polytherapy [12]. In fact several studies have demonstrated the negative impact of polytherapy on the QOL of patients with epilepsy which has been explained by the greater risk for adverse events of antiepileptic drugs [2, 6, 9, 10, 11, 14, 16]. The duration of epilepsy has been determined as an independent predictor of the seizure worries. According to some investigators the greater duration has a positive impact on the QOL because of the better adaptation to the psycho-social consequences of the disease [5]. Gusev et al (2002) however, have demonstrated the negative influence of the greater epilepsy duration on the overall QOL score [9]. Guekht et al (2007) have proven a similar influence on some QOL aspects – energy/fatigue, medication effects, social functioning and overall QOL [8]. Canuet et al (2009) have found an impact of the epilepsy duration on the QOL of elderly patients. Regarding the type of seizures, Gromov et al (2005) have proven that the patients having partial seizures make lower assessments of the physical and mental health in comparison to the patients having generalized seizures [7].

Purpose of the study: To assess the impact of some clinical factors (epilepsy duration, clusters of seizures and/or epileptic status, type of epilepsy, type of seizures, mono-/polytherapy) on the quality of life of Bulgarian patients with refractory epilepsy.

PATIENTS 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.

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: a signed informed consent form; age between 18 and 65 years; a diagnosis of RE; lack of cognitive impairment based on Evaluation Rapide des Fonctions Cognitives (ERFC; Gil and Toullat, 1986) 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; lack of progressive somatic or neurological disease; lack of a simple or complex partial seizure in the last 4 hours; and lack of generalized tonic-clonic seizure in the last 24 hours. Epilepsy was accepted as refractory in cases in which adequate seizure control had not been achieved with at least two potentially effective anti-epileptic drugs prescribed as mono- or poly-therapy at maximally tolerated doses. After excluding 39 patients with pseudo-refractory epilepsy (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 hours or a generalized tonic-clonic seizure in the last 24 hours, 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 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. All study participants completed QOLIE-89. 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 towards epilepsy, physical, mental and social health. QOLIE-89 overall score 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 quality of life. 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 SPSS 13.0. The results for quantitative variables were expressed as the mean ± SE (standard error) and the results for qualitative variables were expressed as percentages. Pearson's correlation coefficient and $\chi 2$ test were used to analyze the correlation between the clinical factors and the assessments of the subscales and the overall score of QOLIE-89.

RESULTS

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

Table 1. Clinical findings of the study participants

	N	P (%)	SE
Type of epilepsy			
– partial	53	75.71	5.11
– generalized	16	22.86	5.03
– not defined	1	1.43	-
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
Clusters and/or epileptic status			
– yes	35	50.00	5.98
– no	35	50.00	5.98
Therapy			
– monotherapy	7	10	3.59
– polytherapy	63	90	3.59

The mean overall score of QOLIE-89, given by the patients with RE, was 64.30 ± 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 of 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 of the epileptic population.

It has been found that the duration of epilepsy has influence only on the subscale “Change in health” $P < 0.05$ ($\chi^2 = 14.17$) – Table 2. In conclusion the greater duration is associated with an unfavorable change in health. A possible explanation of these results is the accumulation of more concomitant diseases.

Table 2. Influence of the epilepsy duration on the assessments of the subscale “Change in health”

Duration of epilepsy	**“Change in health” scores**			**Total**
	≤ 45	**46-55**	**> 55**	
	N (%)	N (%)	N (%)	N (%)
≤ 10 years	0 (0.0%)	3 (37.5%)	5 (62.5%)	8 (100.0%)
11-20 years	8 (29.63%)	15 (55.56%)	4 (14.81%)	27 (100.0%)
21-30 years	2 (8.0%)	13 (52.0%)	10 (40.0%)	25 (100.0%)
> 30 years	12 (35.29%)	13 (38.24%)	9 (26.47%)	34 (100.0%)
Total	22 (23.40%)	44 (46.81%)	28 (29.79%)	94 (100.0%)

The clusters of seizures and/or epileptic status have a negative impact on the assessments of the subscale “Sexual relations” $P < 0.05$ ($\chi^2 = 8.47$). Of the patients without such clinical manifestations 25% gave very low and low scores for this subscale; 29.2% gave high scores. 54.3% of the patients having seizure clusters and/or epileptic status gave very low and low scores, only 17.4% gave high scores $P < 0.01$ ($r_{xy} = -0.29$).

An impact of the type of epilepsy on the assessments of the subscale “Seizure worry” has been demonstrated $P < 0.05$ ($\chi^2 = 9.48$). Approximately 50% of the 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. 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 has been proven as well, $P < 0.05$ ($\chi^2 = 9.67$) – Table 3. As a whole the overall score of QOLIE-89 was lower in patients having partial epilepsy.

Table 3. Overall score of QOLIE-89 depending on the type of epilepsy

Type of epilepsy	**Overall score of QOLIE-89**				**Total**
	≤ 35	**36-45**	**46-55**	**> 55**	
	N (%)	N (%)	N (%)	N (%)	N (%)
Partial	10 (14.93%)	18 (26.87%)	23 (34.33%)	16 (23.87%)	67 (100.0%)
Generalized	8 (38.10%)	2 (9.52%)	3 (14.28%)	8 (38.10%)	21 (100.0%)
Total	18 (20.45%)	20 (22.73%)	26 (29.55%)	24 (27.27%)	88 (100.0%)

An impact of the seizure type on the subscale “Overall health” has been demonstrated $P < 0.05$ ($\chi^2 = 26.06$). 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 the 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.

An impact of the number of antiepileptic drugs applied recently (mono-/polytherapy) on the assessments of the subscale “Overall health” has been found, $P < 0.05$ ($\chi^2 = 8.53$) – Table 4. An interesting result is the more frequent high scores given by the patients on polytherapy, $P < 0.01$ ($r_{xy} = 0.22$), which could be probably explained by a feeling of greater safety about having seizures.

Table 4. Assessments of the subscale “Overall health” depending on the recent treatment with mono-/polytherapy

Recent therapy	**“Overall health” – scores**				**Total**
	≤ 35	**36-45**	**46-55**	**> 55**	
	N (%)	N (%)	N (%)	N (%)	N (%)
Monotherapy	6 (50.0%)	1 (8.33%)	2 (16.67%)	3 (25.0%)	12 (100.0%)
Polytherapy	12 (14.63%)	14 (17.07%)	26 (31.71%)	30 (36.59%)	82.0 (100.0%)
Total	18 (19.15%)	15 (15.96%)	28 (29.79%)	33 (35.10%)	94 (100.0%)

DISCUSSION

The purpose of our study was to assess the impact of some clinical factors (duration of epilepsy, clusters of seizures and/or epileptic status, type of epilepsy, type of seizures, mono-/ polytherapy) on the quality of life of Bulgarian patients with RE. The study results have demonstrated the impact of all clinical factors on some aspects of the QOL of these patients. The greater duration of epilepsy has a negative impact on the assessments of the change in health during the last year – 35.3% of the patients with epilepsy duration greater than 30 years gave very low and low scores. A number of investigators have shown the negative influence of the great duration of epilepsy on the overall score of the QOL [5, 7, 8, 10, 12] and/or some of its aspects – energy/fatigue, medication effects, social functioning, overall QOL [8], the subjective estimation of cognitive impairment and tiredness [1].

A correlation of seizure clusters and/or epileptic status in the disease course with lower assessments of the sexual relations has been found – 54.3% of the patients with these clinical characteristics gave very low and low scores for this subscale. Data about that sort of a correlation were not found in literature sources.

An impact of the type of epilepsy has been found on: 1. Seizure worries – the participants with generalized epilepsy had less worries (45% of them gave high scores); 2. The overall score of QOLIE-89 – the patients with partial epilepsy had lower scores (41.8% gave very low and low scores, 29.3% – high scores). Sanjeev et al (2005) have also found a lower overall score of QOLIE-31 in patients having partial epilepsy [14]. Canuet et al (2009) have determined the type of epilepsy as a predictor for the assessment of other subscales – “Emotional well-being” and “Energy/fatigue” [3].

An impact of the seizure type on the subscale “Overall health” has been demonstrated. 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% of them gave very low and low scores). The greatest percentage of high scores (40.91%) were given by the participants having generalized tonic-clonic seizures, generalized myoclonic seizures, and polymorphic seizures (40.43%). These results are similar to the ones obtained by Gusev et al (2002). They have found lower QOL assessments in the patients with secondarily generalized seizures compared to the assessments of the participants with partial seizures without secondary generalization [9]. In contrast to our results, Velizarova (2007) has obtained lower QOL scores from patients with complex partial seizures compared to the scores of participants with secondarily generalized seizures [1].

An impact of the prescribed treatment as mono-/polytherapy on the assessments of the overall health has been demonstrated – the scores were higher in cases with polytherapy (36.59%). These results differ from the results in literature sources of a higher QOL in cases with monotherapy [4, 9, 12, 14] which can be explained by special features of Bulgarian patients' mentality associated with a feeling of safety while using more drugs. Tracy et al. (2007) have demonstrated lower scores for the QOLIE-31 subscale "Cognitive" in cases with polytherapy [15]. Pirio Richardson et al (2004) have discovered a significant improvement of the assessments of the following QOL aspects in cases of reducing polytherapy to monotherapy: memory impairment, worries about medication effects, difficulties in the drugs intake and recreational activities, overall health [13].

LIMITATIONS

The first limitation of our study is that only patients with RE completed QOLIE-89. We excluded patients older than 65 years, having cognitive impairment, progressive neurological disease, and those with simple or complex partial seizures in the last 4 hours or generalized tonic-clonic seizures in the last 24 hours with the purpose of an adequate completion of QOLIE-89. The participation of no other patients but only those having access to the University Clinic of Neurology, who usually attended it for a regular examination or in cases of unsatisfactory seizure control or adverse events from treatment, is also a limitation. 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.

In conclusion, the demonstration of the role of the rarely studied clinical factors epilepsy duration, clusters of seizures and/or epileptic status, type of epilepsy, type of seizures, mono-/polytherapy for the QOL in cases with RE contributes to clarifying the significance of more QOL predictors, despite their impact on single aspects. The investigation of the impact of the described factors will be useful for making a more complex estimation of patients' problems and focusing medical efforts on overcoming them. Being able to predict and address these issues will motivate the medical community to study all QOL predictors more profoundly, to limit their influence, and improve the patients' quality of life.

REFERENCES

1. Velizarova-Stoimenova, R. Cognitive impairment in focal epilepsies [dissertation]. – Medical University – Sofia, 2007 (in Bulgarian).

2. Aydemir, N. et al. Changes in quality of life and self-perspective related to surgery in patients with temporal lobe epilepsy. – Epilepsy Behav, **5**, 2004, № 5, 735-742.
3. Canuet, L. et al. Factors associated with impaired quality of life in younger and older adults with epilepsy. – Epilepsy Res., **83**, 2009, № 1, 58-65.
4. Choi-Kwon, S. et al. Factors affecting quality of life in patients with epilepsy in Seoul, South Korea. – Acta Neurol. Scand, **108**, 2003, № 6, 428-434.
5. Djibuti, M. et R. Shakarishvili. Influence of clinical, demographic and socioeconomic variables on quality of life in patients with epilepsy: findings from Georgian study. – J. Neurol. Neurosurg. Psychiatry, **74**, 2003, № 5, 570-573.
6. Gilliam, F. Optimizing health outcomes in active epilepsy. – Neurology, **58**, 2002, № 8, Suppl. 5, S9-20.
7. Gromov, S., V. Mikhailov et S. Tabulina. Epilepsy and quality of life in patients in the course of their treatment rehabilitation. – Epilepsia, **46**, 2005, № 6, 185.
8. Guekht, A. B. et al. Factors influencing on quality of life in people with epilepsy. – Seizure, **16**, 2007, № 2, 128-133.
9. Gusev, E. L. et al. Quality of life (QOL) in patients with symptomatic localisation related epilepsies (SLE). – Epilepsia, **43**, 2002, № 8, 199.
10. Johnson, E. K. et al. The relative impact of anxiety, depression and clinical features on health-related quality of life in epilepsy. – Epilepsia, **45**, 2004, № 4, 544-550.
11. Kiiskinen, P. et al. Model of comprehensive care and support to prevent isolation in people with epilepsy. – Epilepsia, **43**, 2002, № 8, 61.
12. Piperidou, C. et al. Association of demographic, clinical and treatment variables with quality of life of patients with epilepsy in Greece. – Qual. Life Res., **17**, 2008, № 7, 987-996.
13. Pirio Richardson, S. et al. Improvement in seizure control and quality of life in medically refractory epilepsy converted from polytherapy to monotherapy. – Epilepsy Behav, **5**, 2004, № 3, 343-347.
14. Sanjeev, T., K. Samue, S. Nair et S. Sankara. Frequent seizures and polytherapy can impair quality of life in patients with epilepsy. – Neurol. India, **53**, 2005, № 1, 46-50.
15. Tracy, J. L. et al. The association of mood with quality of life ratings in epilepsy. – Neurology, **68**, 2007, № 14, 1101-1107.
16. Villeneuve, N. Quelles échelles de qualité de vie pour les patients ayant une épilepsie partielle pharmacorésistante. – Rev. Neurol. (Paris), **160**, 2004, Spec № 1, 5S376-5S393.
17. Viteva, E., Z. Zachariev et M. Semerdzhieva. Validation of the Bulgarian Version of the Quality of Life Inventory (QOLIE-89). – Folia Med. (Plovdiv), **1**, 2010, № 52, 34-39.

✉ *Address for correspondence:*
Dr. Ekaterina Viteva, Ph.D.
Medical University of Plovdiv
Department of Neurology
15A Vasil Aprilov str.
4002 Plovdiv, Bulgaria
☎ +359887752235
e-mail: kiv14477@yahoo.com