

# IMPACT OF INVASIVE EEG MONITORING AND RESECTIVE NEUROSURGICAL TREATMENT ON THE QUALITY OF LIFE IN PATIENTS WITH DRUG RESISTANT EPILEPSY - PRELIMINARY RESULTS

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received: 12.9.2019;

revised: 21.10.2019;

accepted: 3.12.2019

## SUMMARY

**Background:** Neurosurgical treatment is one of important way to cure drug resistant epilepsy. After invasive EEG monitoring and the invasive neurosurgical treatment (resective surgery) there are possible complications (intracranial haemorrhage, cortical lesions and infections), however there are possible neuropsychologic outcomes such as memory outcomes, language outcomes and psychiatric outcomes. The quality of life in epilepsy (QOLIE-31) scale is a self-completed questionnaire which contains seven subscales which address the following aspects: emotional well-being, social functioning, energy/fatigue, cognitive functioning, seizure worry, medication effects and overall quality of life. Our study aimed to examine the quality of life in patients with drug resistant epilepsy who had undergone invasive EEG monitoring and resective neurosurgical treatment through the application of the QOLIE-31 scale.

**Subjects and methods:** The study included 9 patients with drug resistant epilepsy who had undergone invasive EEG monitoring followed by resective neurosurgical treatment in the period from 2010 to 2016, and the control group of 15 patients with drug resistant epilepsy who had not undergone neurosurgical procedures. Clinical variables of interest for this study were obtained through phone contact, and the QOLIE-31 scale was applied.

**Results:** In the domaine of seizure worry, patients in the examined group were more concerned about the seizures (54.7) compared to the examined group (80), as well as in the overall quality of life (examined group 57.5; control group 77.5). Patients in the control group complained more in the domain of antiepileptic therapy (score 70.7) than patients in the examined group (score 100). In the other domains: emotional well-being, energy/fatigue, cognitive functioning, and social functioning there were minor deviations between the examined and control groups.

**Conclusion:** There was no statistically significant difference between individual QOLIE-31 questionnaires, as well as between the two groups of respondents.

**Key words:** drug resistant epilepsy - invasive EEG monitoring - epilepsy surgery - QOLIE-31

**Abbreviations:** AED - antiepileptic drug; CSF - cerebrospinal fluid; EEG - electroencephalography; MRI - magnetic resonance imaging; QoL - quality of life; QOLIE-31 - quality of life in epilepsy 31; VNS - vagus nerve stimulator

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## INTRODUCTION

Epilepsy is one the most common chronic neurologic disease, affecting about 50 million of patients worldwide, and around 6 million patients in Europe (Hajnšek 2010). The main precondition for successful treatment of epilepsy is a timely etiological evaluation of disease and clinical phenotype verification, but also the earliest start of treatment with appropriate antiepileptic therapy at the optimal dose, with a view to completely stop epileptic seizures. It is estimated that 30% to 40% of pa-

tients suffer from drug resistant epilepsy, a form of epilepsy in which with at least two optimally selected and regularly taken antiepileptics, at an appropriate dose, the complete release of epileptic seizures has not occurred (Hajnšek et al. 2010, Kwan et al. 2010).

An increasing number of studies have shown that surgery of epilepsy plays an important role in the treatment of drug-resistant epilepsy. Moreover, the comprehensive treatment mainly based on surgery can achieve the remission and even cure of drug resistant epilepsy (Sheng 2018).

Very important is careful selection of patients with drug resistant epilepsy who are candidates for preoperative examination before invasive (classic neurosurgical resection) or minimally invasive neurosurgical treatment (implantation of vagus nerve stimulator (VNS) (Schramm et al. 2008, Petelin et al. 2010, Miller et al. 2013, Yamamoto 2015, Sheng 2018). Seizure recurrence after resection follows predictable slopes based on multiple factors, including the duration of epilepsy, history of generalised tonic seizures, frequency of preoperative seizures, and the presumptive pathological cause of epilepsy on magnetic resonance imaging (MRI) (Miller et al. 2013, Yamamoto 2015, Najm 2018). Because of these facts patients with drug resistant epilepsy are candidates for detailed preoperative examination before neurosurgical treatment (Najm 2018).

In the preoperative evaluation of patients with drug resistant epilepsy, diagnostic techniques can be divided into noninvasive and invasive. The invasive EEG monitoring can be performed during surgery to optimise delineation of the epileptogenic area by taking into account interictal spikes and spike patterns while reducing resection volume. This may reduce neurological deficits and yield a better quality of life (McKhann et al. 2000, Schramm et al. 2008, Petelin et al. 2010, Miller et al. 2013, Yamamoto 2015, Najm 2018,).

After the invasive EEG monitoring and neurosurgical treatment (resective surgery) there are possible complications (intracranial haemorrhage, cerebrospinal fluid (CSF) leak, cortical lesions and infections) and neuropsychologic outcomes such as memory outcome, language outcomes and psychiatric outcomes (Fong et al. 2012, Hader et al. 2013, Van 't Klooster et al. 2015).

The Quality of life in epilepsy - (QOLIE-31) is a self-completed questionnaire designed for adult epileptic patients (18 years or older). We used the QOLIE-31 validated Croatian 1.0 version. It contains seven subscales which address the following aspects: emotional well-being, social functioning, energy/fatigue, cognitive functioning, seizure worry, medication effects and overall quality of life (Lušić et al. 2011).

## SUBJECTS AND METHODS

We conducted a cross-sectional study. The study included 9 patients with drug resistant epilepsy who had undergone invasive EEG monitoring followed by resective neurosurgical treatment in the period from 2010 to 2016, and the control group of 15 patients with drug resistant epilepsy who had not undergone neurosurgical procedures. Both groups were followed at the University Hospital Centre Zagreb, Referral Centre for Epilepsy of the Ministry of Health of the Republic of Croatia.

Clinical variables of interest for this study were obtained through phone contact, and the QOLIE-31 scale was applied. The domains examined in QOLIE-31

are: seizure worry (5 questions), overall quality of life (2 questions), emotional well-being (5 questions), energy/fatigue (4 questions), cognitive functioning (6 questions), medication effects (3 questions), social functioning (5 questions), and patients health status (1 questions). The patients answer by circling the appropriate number (1,2,3...) in response to the question, and if he is not sure can write a comment or explanation next to the question asked. Due to the different meaning of the answers to the question asked, a scoring system was developed that involves the conversion of numerical answers to a scale of 0-100 points.

In the case group only 4 patients accepted to participate in our study. All 4 patients had positive brain MRI 3T, focal cortical dysplasia (FCD).

In the control group we collected 15 properly filled QOLIE-31 questionnaires. These were patients with drug resistant epilepsy and with negative brain MRI 3T, in whom the invasive EEG monitoring was not performed.

In the statistical analysis of data we used the Mann-Whitney U test of nonparametric tests for independent samples. All statistical analyses were performed using Statistica version 13 (StatSoft Inc., Tulsa, OK, USA.). The results were considered statistically significant at the  $p < 0.05$ . The study was approved by the Ethics Committee of the University Hospital Centre Zagreb. Each patient signed informed consent to participate in the study.

## RESULTS

The QOLIE-31 questionnaire was completed by 4 patients (2 females, 2 males, mean age 22.5 years) who had undergone invasive EEG monitoring, and by 15 patients (7 females, 8 males, mean age 46 years) in control group. We compared the two groups in terms of personal specifications with similar demographic characteristics (education, working status, marital status and place of living).

According to the degree of education in the examined group, there were patients with secondary education, of which 2 were active and 2 unemployed. All 4 patients did not have marital cohabitation (2 married, 2 unmarriages), but all had a place of living (2-house / 2 -apartment).

According to the level of education in the control group, most of the patients were with high school education (8) and work-active (9), but there were patients with higher (1) and higher education (1) and also special needs school (1). According to marital status, 6 patients were married and 6 were single (2 unmarried / 1 unmarried, 1 widowed, 1 divorced), and the majority had a place of living (5 house / 7 apartment) (Table 1).

We studied the difference among QOLIE-31 domains between the patients undergoing invasive EEG monitoring and those who did not. The test results are listed in Table 2.

**Table 1.** General data of patients

	Examined group	Control group	p
Age*	22.5 (20.5-25)	46 (32-53)	0.014
Gender			0.906
female	2	8	
male	2	7	
Education			0.398
high school education	4	8	
college education	0	1	
high qualification	0	2	
else	0	4	
Marital status			0.031
married	0	6	
not married	4	4	
else	0	5	
Habitation			0.592
house	2	5	
apartment	2	7	
else	0	3	

\*Median (lower quartile-upper quartile)

**Table 2.** QOLIE-31 scale

QOLIE - 31	All (N=19)	Examined group (N=4)	Control group (N=15)	p
Seizure worry	75 (46-93.4)	54.7 (35-83)	80 (55.8-93.4)	0.422
Overall quality of life	77.5 (50-82.5)	57.5 (45-77.5)	77.5 (62.5-82.5)	0.450
Emotional well-being	80 (56-88)	84 (70-88)	80 (44-88)	0.616
Energy/fatigue	60 (42-75)	57.5 (45-65)	60 (45-75)	0.615
Cognitive function	75.5 (60-96.7)	74.7 (58.7-87.6)	80.3 (60-96.7)	0.802
Medication effects	78.7 (44.3-100)	100 (72.2-100)	70.7 (30.3-88.7)	0.096
Social function	86 (75-100)	90.5 (68-97.5)	80 (75-100)	0.762
Overall score	75.3 (63.4-84.1)	76.4 (59.6-82.4)	72.6 (63.4-84.1)	0.802

Median (lower quartile-upper quartile)

In the domain of seizure worry, patients in the examined group were more concerned about the seizures (54.7) compared to the examined group (80), as well as in the overall quality of life (examined group 57.5; control group 77.5).

Patients in the control group complained more in the domain of antiepileptic therapy (score 70.7) than patients in the examined group (score 100). In the other domains: emotional well-being, energy/fatigue, cognitive functioning, and social functioning there were minor deviations between the examined and control groups. However, there were no statistically significant differences between the individual QOLIE-31 questionnaires (this refers to the overall score), both in the total score and in both examined groups ( $p=0.802$ ).

## DISCUSSION

The World Health Organization (WHO) defines the quality of life (QoL) «an individual's perception of their position in the life in the context of the culture and value systems in which they live and concerning their goals, expectations, standards, and concerns» (Jacoby et al. 2009, Mahrer et al. 2013).

There are two types of subjective quality of life measures: generic and disease specific measures. While generic measures can be applied to a wide variety of patients, specific instruments are focused on issues related to the individual disease states or patient groups (Duka Glavor et al. 2019).

In assessing the QoL of patients with epilepsy, the emphasis is placed on the factors that have the greatest influence on the QoL of patients with epilepsy such as: time of first seizure, seizure frequency, seizure type, the efficacy of treatment with antiepileptic drugs and undesirable effects of antiepileptic drugs (Guekht et al. 2007, Jacoby et al. 2009, Mahrer-Imhof et al. 2013). Mood disorders represent a frequent psychiatric comorbidity in epilepsy with adverse consequences for health-related quality of life (Wiglusz et al. 2012).

One of the important factors is also the influence of preoperative and operative treatment on the QoL of patients with drug resistant epilepsy. One way to monitor the effect of preoperative treatment and applied treatment on the QoL of patients with drug resistant epilepsy is through the questionnaire such as QOLIE-31.

The goal of resective epilepsy surgery is long-term seizure freedom. Seizure-free rates are lower in patients with nonlesional neocortical resections. Epileptogenic zones are often distributed in the cortex, but vary from person to person, and sometimes may reside in the deep structure of the brain (Blümcke 2011, Petelin Gadže 2017). Surgical management of extratemporal lobe epilepsy is mainly applicable for patients who had drug resistant epilepsy induced by focal cortical dysplasias (FCD) (Blümcke 2011).

FCD may be subtle, sometimes meticulous inspection will reveal mild cortical thickening or an unusually deep sulcus, but special image analysis techniques can help (Blümcke 2011). Invasive video-EEG can more precisely delineate the extent of a neocortical epileptogenic zone and its relationship to areas of the eloquent functional cortex (Blümcke 2011).

Quality of life in patients with drug resistant epilepsy improved after surgery of FCD, but improved the most in patients who were seizure-free following surgery (Blümcke 2011, Mohammed et al. 2012, Jobst et al. 2015).

In our prospective clinical cross-sectional study we have reported the short outcomes of QoL questionnaire, QOLIE-31, concerning clinical variables - seizure worry, overall quality of life, emotional well-being, energy/fatigue, cognitive function, medication effects and social function. We studied the difference among QOLIE-31 domains between the patients undergoing invasive EEG monitoring and those who did not. Depending on the present data patients in the examined group were more concerned about the seizures (54.7), and in the overall quality of life (57.5), compared to the examined group, but there was no statistically significant difference between individual QOLIE-31 questionnaires, as well as between the two groups of respondents.

Apart from the study of McKhann et al. 2000 on the importance of performing invasive EEG monitoring, and the study of Fong et al. 2012, and Hader et al. 2013 on possible complications after performing invasive EEG monitoring such as bleeding, CSF leak, ischemic lesions or infections, we did not find any published study that would investigate the quality of life of patients with drug resistant epilepsy following invasive EEG monitoring and using scale QOLIE - 31 that we can compare with our results. In our group of patients, during and after invasive EEG monitoring, there were no complications after performed treatment.

## CONCLUSION

The presented study is the first of its kind to investigate the impact of invasive EEG monitoring followed by resective neurosurgical treatment on the quality of life in patients with drug resistant epilepsy using the scale QOLIE - 31.

During and after the invasive EEG monitoring, there were no complications in the sense of bleeding, ischemic lesions or infections after the performed treatment. There was no statistically significant difference between individual QOLIE-31 questionnaires, as well as between the two groups of respondents.

At this time we cannot conclude that there is a significant difference in the QOLIE 31 in those patients compared to the group of patients with drug resistant epilepsy who had not undergone neurosurgical procedures. Therefore, we will continue to follow QOLIE-31 in our patients and include a new one in the study in the future.

## Acknowledgements:

We are thankful to our colleagues for their support in this research:

*University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Department of Neurology, Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy:* Assoc. Prof. S. Hajnšek, M.D., Ph.D.; Prof. Z. Poljakovic, M.D., Ph.D.; S. Nankovic, M.D.; V. Sulentic, M.D.; I. Cajic, M.D.; A Bujan Kovac, M.D.; Assist. Prof. M. Krbot Skoric, EE., Ph.D.; Assist. Prof. V. Isgum EE, Ph.D.

*University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Department of Diagnostic and Interventional Radiology:* Assoc. Prof. Marko Rados, M.D., Ph.D.; Assoc. Prof. Milan Rados, M.D., Ph.D.; Assist. Prof. D. Ozretic M.D., Ph.D.; Assist. Prof. G Pavlisa, M.D., Ph.D.

*University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Department of Neurosurgery:* Prof. Josip Paladino, M.D., Ph.D.; Andrej Desnica, M.D.; Jakob Nemir, M.D., Ph.D.

*University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Medical Library Rebrow:* Prof. Arijana Hajnšek Čaklec.

*University Hospital Centre Split, Department of Neurology:* Prof. Lidija Sodici, M.D., Ph.D.

**Conflict of interest :** None to declare.

## Contribution of individual authors:

*Dragana Mijatović:* study desing of the article, data collection, literature searches, writing the manuscript, statistical analysis and interpretation of results, approval of the final version.

*Željka Petelin Gadže:* study desing, revisioning the manuscript, approval of the final version.

*Filip Đerke:* data collection, literature searches, approval of the final version.

*Goran Mrak:* revisioning the manuscript, approval of the final version.

*Ratimir Petrović:* revisioning the manuscript, approval of the final version.

*Andrica Lekić:* statistical analysis and interpretation of results, approval of the final version.

## References

1. Blümcke I: *The clinicopathologic spectrum of focal cortical dysplasias: a consensus classification proposed by an ad hoc Task Force of the ILAE Diagnostic Methods Commission. Epilepsia* 2011; 52:158-74. <http://doi.org/10.1111/j.1528-1167.2010.02777>
2. Duka Glavor K, Titlić M & Vuletić G: *Quality of life and health of patients in early stages of multiple sclerosis. Psychiatr Danub* 2019; 31(Suppl 1):S118-S125, *Medicina Academica Mostariensia* 2018; 6:118-125
3. Fong JS, Alexopoulos AV, Bingaman WE et al: *Pathologic Findings Associated With Invasive EEG Monitoring for Medically Intractable Epilepsy, Am J Clin Pathol* 2012; 138:506-510 <https://doi.org/10.1309/ajcpgsnl9vbnjmx>
4. Guekht AB, Mitrokhina TV, Lebedeva AV: *Factors influencing on quality of life in people with epilepsy. Seizure* 2007; 16:128-33. <https://doi.org/10.1016/j.seizure.2006.10.011>
5. Hader WJ, Tellez-Zenteno J, Metcalfe A et al: *Complications of epilepsy surgery: a systematic review of focal surgical resections and invasive EEG monitoring. Epilepsia* 2013; 54:840-847. <https://doi.org/10.1111/epi.12161>
6. Hajnšek S: *Epilepsije: klasifikacija i klinička slika. Neurol Croatica* 2010; 59:5-21
7. Hajnšek S, Kovačević I, Petelin Ž: *Epilepsy - therapeutic guidelines. Neurol Croatica* 2010; 59:35-62
8. Jacoby A, Snape D, Baker GA: *Determinants of quality of life in people with epilepsy. Neurol Clin* 2009; 27:843-863. <https://doi.org/10.1016/j.ncl.2009.06.003>
9. Jobst BC, Cascino GD: *Resective Epilepsy Surgery for Drug-Resistant Focal Epilepsy A Review JAMA* 2015; 313:285-293. <http://doi.org/10.1001/jama.2014.17426>
10. Kwan P, Arzimanoglou A, Berg TA, Brodie JM: *Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies, Epilepsia* 2010; 51:1069-1077
11. Lušić I, Džamonja G, Titlić M et al: *Psychometric Validation of the Croatian Version of the Quality of Life in Epilepsy Inventory (QOLIE-31), University of Split, Split University Hospital Centre, Department of Neurology, Split, Croatia, Coll Antropol* 2011; 35:1177-1184
12. Mahrer-Imhof R, Jaggi S, Bonomo A: *Quality of life in adult patients with epilepsy and their family members. Seizure* 2013; 22:128-35. <https://doi.org/10.1016/j.seizure.2012.11.012>
13. McKhann GM, Schoenfeld-McNeill J, Born DE: *Intra-operative hippocampal electrocorticography to predict the extent of hippocampal resection in temporal lobe epilepsy surgery. J Neurosurg* 2000; 93:44-52. <https://doi.org/10.3171/jns.2000.93.1.0044>
14. Miller JW, Hakimian S: *Surgical treatment of epilepsy. Continuum* 2013; 19(3) *Epilepsy* 2013; 730-742. <https://doi.org/10.1212/01.CON.0000431398.69594.97>
15. Mohammed HS, Kaufman CB, Limbrick DD et al: *Impact of epilepsy surgery on seizure control and quality of life: A 26-year follow-up study. Epilepsia* 2012; 53:712-720. <http://doi.org/10.1111/j.1528-1167.2011.03398.x>
16. Najm IM: *Mapping brain networks in patients with focal epilepsy. Lancet Neurol* 2018; 17:295-297. [https://doi.org/10.1016/S1474-4422\(18\)30090-5](https://doi.org/10.1016/S1474-4422(18)30090-5)
17. Petelin Gadže Ž: *Dijagnostički i terapijski pristup bolesniku s epilepsijom. Medicinska naklada, Zagreb*, 2017; 1-5
18. Petelin Ž, Hajnšek S, Wellmer J, Mrak G, Radoš M, Paladino J: *Guidelines for Preoperative Diagnostic Evaluation of Patients with Pharmacoresistant Epilepsy. Neurol Croatica* 2010; 59:22-34
19. Schramm J, Chusmann H: *The surgery of epilepsy. Neurosurgery* 2008; 62:463-481. <https://doi.org/10.1227/01.neu.0000316250.69898.23>
20. Sheng J: *Drug-Resistant Epilepsy and Surgery. Curr Neuropharmacol* 2018; 16:17-28. <https://doi.org/10.2174/1570159X15666170504123316>
21. Van 't Klooster MA, Leijten FS, Huiskamp G et al.: *HFO study group: High-frequency oscillations in the intra-operative ECoG to guide epilepsy surgery ("The HFO Trial"): study protocol for a randomized controlled trial. Trials* 2015; 23:16:422. <https://doi.org/10.1186/s13063-015-0932-6>
22. Wiglusz MS, Cubala WJ, Galuszko-Wegielnik M, Jakuszkowiak-Wojten K, Landowski J: *Mood disorders in epilepsy - diagnostic and methodological considerations. Psychiatr Danub* 2012; 24(Suppl 1):44-50
23. Yamamoto T: *Vagus nerve stimulation therapy: indications, programming and outcomes. Neurol Med Chir* 2015; 55:407-15. <https://doi.org/10.2176/nmc.ra.2014-0405>

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