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Analysis of incomplete remission cases in post-surgery patients with focal drug-resistant epilepsy

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ABSTRACT

Background. Epilepsy surgery is mainly aimed at removing patient seizures. Despite the high efficiency of surgical treatment, a search for probable predictors of adverse outcomes and the analysis of the quality of life (QoL) in patients attempted to be surgically assisted provide only partial relief from disturbing paroxysms remain relevant.

Objective: To comprehensively assess disease parameters in post-surgery patients with focal drug-resistant epilepsy (DRE) with incomplete remission (Engel II–IV outcomes), and to identify QoL prognostic factors.

Material and methods. A single-center, retrospective, observational study assessing 67 patients with incomplete remission (Engel II–IV outcomes) operated for focal DRE was carried out. The following disease parameters identified as potentially possible QoL predictors after surgical treatment were analyzed: seizure frequency and severity post-surgery; dominance of the brain hemisphere underwent surgery; pre-surgery seizure type; neurological deficit post-surgery; epileptogenic substrate morphology; resection zone; extent of resection; disease duration.

Results. In patients with Engel II–IV surgery outcomes, a quite high level of positive subjective self-assessment condition (52,2%) was revealed, with number of seizures reduced by at least 50% in 59,7% cases. A statistically significant influence on the positive subjective QoL assessment based on criteria such as decreased frequency and strength of seizures after surgery ($p<0,001$) was found. Tailored resection of the epileptogenic zone led to aggravated seizure severity and frequency outcomes. Lobectomies and disconnection operations in 45,7% cases were accompanied by reduced number of seizures by at least 75%. Temporal lobe surgeries, compared with extratemporal resections, were more often correlated with QoL improvement.

Conclusion. In most cases, DRE surgical treatment leads to lower seizure rate and significantly improved QoL, even in the case of incomplete remission. Seizure frequency and severity post-surgery were the only parameters affecting postsurgical QoL in patients with incomplete remission.

KEYWORDS

drug-resistant epilepsy, surgical treatment of epilepsy, incomplete remission, quality of life

For citation

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Анализ случаев неполной ремиссии после хирургического лечения пациентов с фокальной фармакорезистентной эпилепсией

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РЕЗЮМЕ

Введение. Основной целью хирургического лечения эпилепсии является избавление пациента от приступов. Несмотря на высокую эффективность таких операций, остаются актуальными поиск вероятных предикторов неблагоприятных исходов и анализ качества жизни (КЖ) пациентов, попытки помочь которым хирургическими методами приводят лишь к частичному контролю над приступами.

Цель: многофакторная оценка параметров болезни в группе пациентов с фокальной ФРЭ, у которых не удалось достичь контроля над приступами после хирургического лечения (исходы классов II–IV по шкале Engel), и выявление среди них потенциальных предикторов КЖ.

Материал и методы. Проведено одноцентровое ретроспективное наблюдательное исследование, в которое включены 67 пациентов с неполной ремиссией (исходы Engel II–IV), прооперированных по поводу фокальной ФРЭ. Проанализированы особенности течения заболевания, определенные как потенциально возможные предикторы КЖ после хирургического лечения: частота и тяжесть приступов после операции, доминантность полушария, на котором выполнено вмешательство, тип приступов до операции, наличие неврологического дефицита после нее, морфология эпилептогенного субстрата, область оперативного вмешательства, объем резекции, длительность болезни.

Результаты. У пациентов с исходами хирургии Engel II–IV выявлен достаточно высокий уровень позитивной субъективной оценки своего состояния (52,2%) при сокращении количества приступов на 50% и более в 59,7% случаев. Выявлено статистически значимое влияние на субъективную оценку КЖ по таким критериям, как частота и сила приступов после операции ($p<0,001$). Тейлорированная резекция эпилептогенной зоны приводила к худшим результатам по этим параметрам. Лобэктомии и дисконнективные операции в 45,7% случаев сопровождались сокращением количества приступов на 75% и более. Операции на височной доле по сравнению с экстратемпоральными резекциями чаще коррелировали с улучшением КЖ.

Заключение. Хирургическое лечение ФРЭ в большинстве случаев приводит к сокращению количества приступов и значимому улучшению КЖ пациентов даже в случае неполной ремиссии. Параметрами, оказывающими влияние на КЖ при достижении неполной ремиссии, оказались частота и сила приступов после операции.

КЛЮЧЕВЫЕ СЛОВА

фармакорезистентная эпилепсия, хирургическое лечение эпилепсии, неполная ремиссия, качество жизни

Для цитирования

Утяшева А.А., Ивин Н.О., Ишмуратов Е.В., Утяшев Н.П., Гордеева Е.А., Зуев А.А. Анализ случаев неполной ремиссии после хирургического лечения пациентов с фокальной фармакорезистентной эпилепсией. *Эпилепсия и пароксизмальные состояния.* 2025; 17 (1): 27–39. https://doi.org/10.17749/2077-8333/epi.par.con.2025.199.

INTRODUCTION / ВВЕДЕНИЕ

According to the World Health Organization, more than 50 million people worldwide suffer from epilepsy, about 5 million new cases are detected annually, allowing to consider this disease as one of the most common [1] thereby creating a serious national financial burden. The tangible economic consequences are caused by patients' need for medical care, reduced working capacity and labor productivity, since epilepsy accounts for more than 0.5–0.7% of the global disease burden. The latter combines the probability of premature death, as well as years of life in poor health at a certain time point [1, 2].

In addition to its socio-economic significance, epilepsy affects each patient individually and carries potential difficulties in social relationships, employment, independent life, as well as also impair mental and physical health [3–5]. Many specialists dealing with epilepsy note that the quality of life (QoL) of patients suffering from this disease changes dramatically [3, 5].

Treatment of epilepsy is aimed not only at improving QoL, but also at reducing the overall mortality rate, because the risk of sudden premature death in epilepsy alone comprises 1.16 cases per 1000 people [6], which is about 3 times higher than in the general population [7].

According to the observations of the International League Against Epilepsy (ILAE), the probability of response to drug therapy in a patient with newly diagnosed epilepsy prescribed the first properly selected anticonvulsant drug was 49.5%, the second – 36%, the cumulative effectiveness of all subsequent drugs does not exceed 12.5–22.2% [8]. In case of conservative therapy ineffective in patients with focal drug-resistant epilepsy, it is recommended to consider an opportunity of applying surgical treatment, since the probability of being seizure-free post-surgery is 2.5 times higher than in patients continuing to receive pharmacotherapy alone [9].

The main goal of epilepsy surgery is either to free a patient of seizures completely or to reduce their frequency and severity. While planning surgical treatment, it is of particular importance to minimize potential surgical complications and

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predicted neurological deficits, which also affect QoL [10]. To date, the effectiveness of epilepsy surgical treatment is estimated to be quite high ranging from 34% to 85% so that patients can be completely cured of epileptic seizures [10–12].

Given the high surgery efficiency, most relevant studies pay attention to patients with favorable outcomes. This approach is probably justified by the need to define criteria to select candidate patients for surgical treatment and to understand the concepts of their follow-up. Currently, it remains relevant to seek out for probable predictors of adverse outcomes and analyze QoL in patients with partial relief from disturbing paroxysms post-surgery.

Objective: To comprehensively assess disease parameters in post-surgery patients with focal drug-resistant epilepsy (DRE) with incomplete remission (Engel II–IV outcomes), and to identify QoL prognostic factors.

MATERIAL AND METHODS / МАТЕРИАЛ И МЕТОДЫ

A single-center retrospective observational study enrolled patients with recurrent epileptic seizures post-surgery. Patients with focal DRE underwent surgical interventions (340 total) from March 2016 to June 2022, performed at the National Medical and Surgical Center named after N.I. Pirogov, of which 34 (10%) patients a vagus nerve stimulator (VNS) installed due to the lack of indications for resection surgery.

Inclusion and exclusion criteria / Критерии включения и исключения

The study inclusion criteria were as follows:

– verified diagnosis of focal symptomatic epilepsy (G40.1, G40.2 according to the International Classification of Diseases 10th revision);

– age 18 years or more;

– preoperative examination and resection surgery for epilepsy treatment;

– catamnesis tracked for 2 years or more;

– recurrence of epileptic seizures post-surgery;

– signed informed consent.

The study non-inclusion criterion: a patient achieved an Engel I outcome after epileptic seizure recurrence in postoperative period (e.g., due to drug therapy selection).

Exclusion criteria:

– relapse of seizures due to anticonvulsant drug self-withdrawal without medical supervision or other actions that potentially hinder remission achievement (e.g., alcohol consumption);

– identification of persistent psychogenic non-epileptic paroxysms during follow-up postoperative examination;

– refusal to participate in the study.

Pre-surgery examination / Предоперационное обследование

Before surgery, all patients underwent a detailed examination, including neurological status, prolonged electroencephalographic (EEG) video monitoring with registration of typical epileptic seizures using XLTEK (Natus, Canada), Brain Quick (Micromed, Italy), EB-neuro (Galileo, Italy), brain magnetic resonance imaging according to the epileptological protocol using 3 Tl tomograph (Siemens, Germany).

In some patients, in case exact localization of epileptogenic zone might not be determined based on standard methods, additional examinations were performed: positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose, single-photon emission computed tomography (SPECT) according to the SISCOM protocol (subtraction of ictal SPECT co-registered to MRI) (GE Healthcare, USA), prolonged invasive video EEG monitoring with depth electrodes implantation (XLTEK, Brain Quick, EB-neuro).

The decision on surgical intervention was made based on the conclusion drawn by multidisciplinary council of neurologists, epileptologists, neurosurgeons, and neuroradiologists.

Surgery / Хирургическое лечение

In case a single lobe of the brain was involved in the epileptogenic process, lobectomy was the operation of choice. Tailored resections were performed in case epileptogenic substrate was precisely determined according to neuroimaging and neurophysiological examination data, and in some cases epileptogenic substrates were localized within more than one lobe of the brain. In addition, more extensive operations were performed, such as temporal lobectomy combined with tailored resection in another lobe within one hemisphere and disconnection operations, including posterior quadrant disconnection and hemispherotomy.

Intraoperative mapping was performed during surgical interventions in functional zones. The risk of developing neurological deficits was discussed with each patient in case of surgical intervention near functional areas.

Послеоперационная оценка / Post-surgery assessment

Postoperative assessment was performed 6 and 12 months post-surgery and thereafter annually based on follow-up patient hospitalizations and via a telephone survey, which included standard questions regarding general condition, seizure frequency and severity, and anticonvulsant therapy.

The outcomes of surgical treatment were assessed according to the Engel scale [13]. If, post-surgery, a patient stopped suffering from disabling epileptic seizures that reduced his/her ability to work, the outcome of surgical treatment was classified as Engel class I, in case of rare disabling seizures – as Engel class II. If disabling seizures persisted, but significant improvement occurred during disease course (seizure frequency decreased), the treatment outcome was classified as Engel III, whereas the lack of significant improvement post-surgery – Engel IV.

Because commonly accepted outcome assessment scales cannot always be interpreted unambiguously, and study subject was presented by a group of patients with recurrent seizures post-surgery, seizure frequency before and after surgery was estimated as a percentage based on the following principle: Class I – increased seizure frequency, class II – no change in seizure frequency, classes III, IV and V – seizure

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frequency reduced by 25–50%, 50–75% and more than 75%, respectively.

The neurological deficit was assessed based on patient examination and analysis of neurological status.

Statistical analysis / Статистический анализ

The data within the group of patients with Engel II–IV outcomes post-surgery are presented as frequency of occurrence with percentage values. A possible relationship between selected parameters of disease course and perioperative period and QoL was assessed using the χ^2 criterion for qualitative variables. To assess an effect of such parameters on QoL post-surgery, binominal logistic regression method was used. The dependent variable was presented by patient's subjective post-surgery QoL assessment (improved / not improved). The Jamovi software (version 2.3, The Jamovi project, Australia) was used for data analysis. The threshold level of statistical significance (p) was set <0.05.

RESULTS / РЕЗУЛЬТАТЫ

Surgery outcome assessment / Оценка исходов операции

At least 2-year-long follow-up after epileptogenic zone resection was performed in 264 (77.6%) patients, with median catamnesis comprising 41.8 months (range from 12 to 81 months). Of the 264 patients, 197 (74.62%) had Engel I outcome, whereas 67 (25.38%) patients had seizure recurrence (Engel II–IV outcomes) (**Fig. 1**). Three patients underwent surgery twice, and the outcome of the second operation was taken into account upon data evaluation, because all repeated interventions were performed before reaching the annual catamnesis.

Analysis of factors affecting outcomes and QoL / Анализ факторов, влияющих на исход и КЖ

In order to assess the factors likely to affect outcome and QoL, a group of patients with Engel II–IV outcomes (n=67) was analyzed according to the following criteria (**Table 1**):

– frequency (shown as percentage compared to the baseline before surgery) and severity (based on assessment of duration and/or severity of post–seizure manifestations) of seizures;

– dominance of hemisphere underwent surgery;

– type of seizures before surgery (presence of isolated focal or focal combined with bilateral tonic-clonic);

– presence of neurological deficit (excluding hemianopia in posterior quadrant and hemispheric disconnection, as well as in temporal lobectomy as expected consequence of such operations);

– epileptogenic substrate morphology;

– area of surgical intervention;

– extent of resection;

– disease duration.

Some patients required additional examinations to determine epileptogenic zone: in 5 (7.5%) cases – PET with ^{18}F-fluorodeoxyglucose, in 5 (7.5%) cases – SPECT according to the SISCOM protocol, in 18 (26.9%) cases – continued invasive video EEG monitoring with deep electrodes installation.

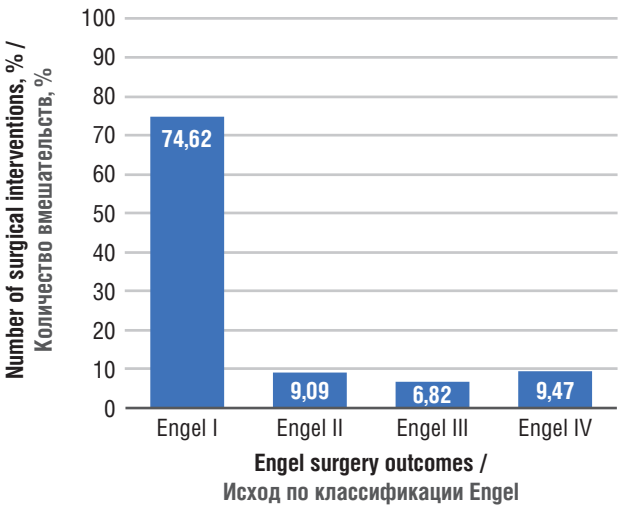

Figure 1. Epilepsy surgery outcomes in patients assisted at the Pirogov National Medical and Surgical Center from March, 2016 to June, 2022 followed up for at least 2 years

Рисунок 1. Исходы хирургических вмешательств по поводу эпилепсии, проведенных в ФГБУ «Национальный медико-хирургический центр им. Н.И. Пирогова» в период с марта 2016 г. по июнь 2022 г., у пациентов с катамнезом 2 года и более

Seizure frequency and severity

The correspondence of the data obtained regarding the frequency of seizures post-surgery and the patients' subjective condition assessment is confirmed by the fact that patients whose frequency of seizures post-surgery did not change rated their condition as "not improved" in 100% of cases (n=13), as well as all patients whose seizures became more frequent post-surgery (n=3), assessed own condition as "deteriorated", the majority of patients whose seizures decreased by more than 75% (n=30; 85.7%), assessed condition as "improved" (**Table 2**).

Hemisphere dominance

The number of patients operated on the dominant (n=34; 50.7%) and subdominant (n=33; 49.3%) hemispheres was commensurate, with no significant correlation found between patients' subjective condition assessment and hemisphere dominance (**Table 3**).

Pre-surgery seizure type

In addition, patients near evenly assessed own condition as "improved" and "not improved" in case of only focal seizures or focal combined with bilateral tonic-clonic seizures pre-surgery (**Table 4**).

In the group with negative outcomes of DRE surgical treatment, patients with former both focal and bilateral tonic-clonic seizures prevailed (73.1%). More than half (53%) of them noted a significant reduction in seizure number (75% or more), however, the majority (61.2%) retained both focal

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Table 1 (beginning). Possible prognostic factors influencing the post-surgery outcome and quality of life in patients with drug-resistant focal epilepsy

Таблица 1 (начало). Вероятные прогностические факторы, влияющие на исход и качество жизни пациентов после хирургического лечения фармакорезистентной фокальной эпилепсии

Parameter / Параметр	Number of patients, n (%) / Число пациентов, n (%)
Seizure number post-surgery / Частота приступов после операции	
increased (class I) / учащение (класс I)	3 (4,5)
no changes (class II) / нет изменений (класс II)	13 (19,4)
reduced by 25–50% (class III) / сокращение на 25–50% (класс III)	11 (16,4)
reduced by 50–75% (class IV) / сокращение на 50–75% (класс IV)	5 (7,5)
reduced by >75% (class V) / сокращение на >75% (класс V)	35 (52,2)
Seizure severity post-surgery / Тяжесть приступов после операции	
milder / стали легче	25 (37,3)
unchanged / остались прежними	36 (53,7)
more severe / стали тяжелее	6 (9,0)
Brain hemisphere dominance for surgical intervention / Доминантность полушария оперативного вмешательства	
dominant / доминантное	34 (50,7)
sub-dominant / субдоминантное	33 (49,3)
Seizure type pre-surgery / Тип приступов до операции	
isolated focal / изолированно фокальные	18 (26,9)
focal combined with BTCS / фокальные в сочетании с БТКП	49 (73,1)
Post-surgery neurological deficit / Послеоперационный неврологический дефицит	
none / отсутствует	62 (92,5)
stable (motor, cognitive) / стойкий (моторный, когнитивный)	5 (7,5)
Region of surgical intervention / Область оперативного вмешательства	
temporal lobe / височная доля	36 (53,7)
frontal lobe / лобная доля	7 (10,4)
parietal lobe / теменная доля	5 (7,5)
insula / инсула	0 (0,0)
occipital lobe / затылочная доля	3 (4,5)
>1 lobes / >1 доли	16 (23,9)
Epileptogenic substrate morphology / Морфология эпилептогенного субстрата	
hippocampal sclerosis / склероз гиппокампа	18 (26,9)
FCD (type 1 and 2) / ФКД (1-й и 2-й типы)	16 (23,9)
FCD (type 3) / ФКД (3-й тип)	6 (9,0)
cystic-gliotic changes / кистозно-глиозные изменения	13 (19,4)
polymicrogyria / полимикрогирия	5 (7,4)
encephalocele / энцефалоцеле	5 (7,4)
glioneuronal tumors (ganglioglioma, DNET) / глионейрональные опухоли (ганглиоглиома, ДНЭО)	4 (6,0)
Resection extent / Объем резекции	
tailored unilobular / тейлорированная в пределах 1 доли	19 (28,3)
tailored multilobular / тейлорированная >1 доли	6 (8,9)
temporal lobectomy / височная лобэктомия	32 (47,8)
temporal lobectomy + tailored multilobular unihemispheric / височная лобэктомия + тейлорированная резекция на другой доле головного мозга в пределах 1 полушария	5 (7,5)
Epilepsy duration / Длительность эпилепсии	
<5 years / <5 лет	4 (6,0)
5–9 years / 5–9 лет	8 (11,9)
10–19 years / 10–19 лет	19 (28,4)
≥20 years / ≥20 лет	36 (53,7)

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Table 1 (end). Possible prognostic factors influencing the post-surgery outcome and quality of life in patients with drug-resistant focal epilepsy

Таблица 1 (окончание). Вероятные прогностические факторы, влияющие на исход и качество жизни пациентов после хирургического лечения фармакорезистентной фокальной эпилепсии

Parameter / Параметр	Number of patients, n (%) / Число пациентов, n (%)
MRI changes detected / Наличие изменений на МРТ	
MR– / MP–	5 (7,5)
MR+ / MP+	62 (92,5)
including bilateral changes / в т.ч. двусторонние изменения	9 (13,4)

Note. *BTCS – bilateral tonic-clonic seizures; FCD – focal cortical dysplasia (the FCD classification according to I. Blümcke et al. [14] was used for assessment); DNET – dysembryoplastic neuroepithelial tumor; MRI – magnetic resonance imaging.*

Примечание. *БТКП – билатеральные тонико-клонические приступы; ФКД – фокальная кортикальная дисплазия (для оценки использована классификация ФКД по I. Blümcke et al. [14]) ДНЭО – дизэмбриопластическая нейроэпителиальная опухоль; МРТ – магнитно-резонансная томография.*

Table 2. A relation between quality of life (QoL) and frequency of seizures in patients with Engel II–IV outcomes post-epilepsy surgery (n=67), n (%)

Таблица 2. Зависимость качества жизни (КЖ) от частоты приступов у пациентов с исходами Engel II–IV после хирургического лечения эпилепсии (n=67), n (%)

Subjective QoL assessment / Субъективная оценка КЖ	Seizure frequency post-surgery / Частота приступов после операции				
	More frequent (class I) / Учащение (класс I) (n=3)	Unchanged (class II) / Без изменений (класс II) (n=13)	Reduced by 25–50% (class III) / Сокращение на 25–50% (класс III) (n=11)	Reduced by 50–75% (class IV) / Сокращение на 50–75% (класс IV) (n=5)	Reduced by >75% (class V) / Сокращение на >75% (класс V) (n=35)
Improvement / Улучшение	0 (0)	0 (0)	3 (27,3)	2 (40)	30 (85,7)
Unchanged / Без изменений	0 (0)	13 (100)	8 (72,7)	3 (60)	5 (14,3)
Aggravation / Ухудшение	3 (100)	0 (0)	0 (0,0)	0 (0)	0 (0,0)

Table 3. Self-patients assessed condition based on surgically treated hemisphere dominance (n=67), n (%)

Таблица 3. Оценка пациентами своего состояния в зависимости от доминантности полушария, на котором проводилась операция (n=67), n (%)

Subjective QoL assessment / Субъективная оценка КЖ	Hemisphere / Полушарие	
	Dominant / Доминантное (n=34)	Sub-dominant / Субдоминантное (n=33)
Improvement / Улучшение	16 (47,1)	19 (57,6)
Unchanged / Без изменений	17 (50,0)	12 (36,4)
Aggravation / Ухудшение	1 (2,9)	2 (6,0)

Note. *QoL – quality of life.*

Примечание. *КЖ – качество жизни.*

Table 4. Self-patient assessed condition post-surgery based on seizures type (n=67), n (%)

Таблица 4. Оценка пациентами своего состояния после операции в зависимости от типа приступов (n=67), n (%)

Subjective QoL assessment / Субъективная оценка КЖ	Типы приступов до операции / Pre-surgery seizure type	
	Isolated focal / Изолированно фокальные (n=18)	Focal combined with BTCS / Фокальные в сочетании с БТКП (n=49)
Improvement / Улучшение	9 (50,0)	26 (53,0)
Unchanged / Без изменений	8 (44,4)	21 (42,9)
Aggravation / Ухудшение	1 (5,6)	2 (4,1)

Note. *QoL – quality of life; BTCS – bilateral tonic-clonic seizures.*

Примечание. *КЖ – качество жизни; БТКП – билатеральные тонико-клонические приступы.*

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and bilateral tonic-clonic seizures (clinically they remained the same as pre-surgery), and 38.8% of seizures subjectively became less severe (bilateral tonic-clonic seizures decreased or reduced). Patients who reported exclusively focal epileptic seizures pre-surgery reported a reduction in their number by 75% or more in 50% of cases, and 66.7% of patients noted that seizures were "less severe", i.e., their duration and/or severity of post-seizure manifestations alleviated (**Table 5**).

Neurological deficit

Patients without neurological deficits after surgical treatment of epilepsy assessed own QoL positively and negatively at near even frequency. Despite the neurological deficits acquired after brain surgery, 8.6% of patients who noted improved QoL post-surgery had persistent motor or cognitive neurological deficits (**Table 6**).

Epileptogenic substrate localization

Among patients with Engel II–IV outcomes who rated own QoL as "improved" and "not improved", 18 (51.4%) and 18 (62.2%), respectively, underwent surgery for epileptogenic lesion localized in the temporal lobe. At the same time, none of the patients after temporal lobe resection (lobectomy, tailored resections) noted QoL deterioration compared to that before surgery.

Among patients with extratemporal resections, 7 (20%) people noted “improved” QoL (2 with frontal lobe resection, 4 – in parietal, 1 – in occipital), 5 (17.1%) – “not improved” QoL (3 with frontal lobe resection, 1 – in parietal, 1 – in occipital), and 3 (100%) patients with QoL deterioration due to increased frequency of epileptic seizures also had extratemporal localization of epileptogenic zone.

It should be noted that among patients with improved QoL, despite persistent epileptic seizures, 28.6% patients who underwent surgery for extensive epileptogenic zones localized in more than one brain lobe (extensive tailored resections, lobectomies combined with tailored resection on another lobe within one hemisphere and disconnection operations) (**Table 7**).

Epileptogenic substrate morphology

The most frequently detected pathomorphological substrates in the presented study group were hippocampal sclerosis found in 18 (26.9%) cases, type 1 and type 2 focal cortical dysplasia (FCD) – in 16 (23.9%), cystic-gliotic changes – in 13 (19.4%). Type 3 FCD (6 (9%) cases), encephalocele and polymicrogyria (5 (7.4%) cases in each group), and glioneuronal tumors (4 (6.0%) cases) were significantly less common (see Table 1). Hippocampal sclerosis and cystic-gliotic changes correlated with lower follow-up seizure frequency, and operations for FCD more often led to unsatisfactory results (**Table 8**).

Resection extent

Despite that all cases of higher seizure frequency after surgical treatment of epilepsy were noted due to tailored re-

Table 5. Pre- and post-surgery seizure characteristics (n=67), n (%)

Таблица 5. Характеристика приступов до и после оперативного лечения (n=67), n (%)

Post-surgery seizure characteristics / Характеристика приступов после операции	Pre-surgery seizure type / Типы приступов до операции	
	Focal / Фокальные (n=18)	Focal combined with BTCS / Фокальные в сочетании с БТКП (n=49)
More frequent / Учащение	1 (5,6)	2 (4,1)
Unchanged / Без изменений	6 (33,3)	7 (14,3)
Reduced by 25–50% / Сокращение на 25–50%	0 (0,0)	11 (22,5)
Reduced by 50–75% / Сокращение на 50–75%	2 (11,1)	3 (6,1)
Reduced by >75% / Сокращение на >75%	9 (50,0)	26 (53,0)
Seizures alleviated / Приступы стали легче	6 (33,3)	19 (38,8)
Seizures not alleviated / Приступы не стали легче	12 (66,7)	30 (61,2)

Note. *BTCS – bilateral tonic-clonic seizures.*

Примечание. *БТКП – билатеральные тонико-клонические приступы.*

Table 6. Quality of life (QoL) for patients with Engel II–IV outcomes in relation to present/absent neurological deficit post-surgery (n=67), n (%)

Таблица 6. Качество жизни (КЖ) пациентов с исходами Engel II–IV в зависимости от наличия/отсутствия неврологического дефицита после операции (n=67) , n (%)

Post-surgery neurological deficit / Послеоперационный неврологический дефицит	Subjective QoL assessment / Субъективная оценка КЖ		
	Improvement / Улучшение (n=35)	Unchanged / Без изменений (n=29)	Aggravation / Ухудшение (n=3)
None / Отсутствует	32 (91,4)	24 (82,7)	3 (100)
Sustained / Стойкий	3 (8,6)	5 (17,3)	0 (0)

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Table 7. Patient subjective quality of life (QoL) assessment in Engel II–IV outcomes post-epilepsy surgery in relation to epileptogenic zone localization (n=67), n (%)

Таблица 7. Субъективная оценка качества жизни (КЖ) пациентами с исходами хирургического лечения эпилепсии Engel II–IV при локализациях эпилептогенной зоны в различных областях головного мозга (n=67), n (%)

Area of surgical intervention / Область оперативного вмешательства	Subjective QoL assessment / Субъективная оценка КЖ		
	Improvement / Улучшение (n=35)	Unchanged / Без изменений (n=29)	Aggravation / Ухудшение (n=3)
Temporal lobe / Височная доля	18 (51,4)	18 (62,2)	0 (0,0)
Frontal lobe / Лобная доля	2 (5,7)	3 (10,3)	2 (66,7)
Parietal lobe / Теменная доля	4 (11,4)	1 (3,4)	0 (0,0)
Occipital lobe / Затылочная доля	1 (2,9)	1 (3,4)	1 (33,3)
>1 lobes / >1 доли	10 (28,6)	6 (20,7)	0 (0,0)

Table 8. Correlation between epileptogenic substrate morphology and seizure frequency post-surgery (n=67), n (%)

Таблица 8. Соотношение морфологии эпилептогенных субстратов и частоты приступов после операции (n=67), n (%)

Epileptogenic substrate morphology / Морфология эпилептогенного субстрата	Seizure number post-surgery / Количество приступов после операции				
	More frequent (class I) / Учащение (класс I) (n=3)	Unchanged (class II) / Без изменений (класс II) (n=13)	Reduced by 25–50% (class III) / Сокращение на 25–50% (класс III) (n=11)	Reduced by 50–75% (class IV) / Сокращение на 50–75% (класс IV) (n=5)	Reduced by >75% (class V) / Сокращение на >75% (класс V) (n=35)
Hippocampal sclerosis / Склероз гиппокампа	0	2 (15,4)	6 (54,5)	1 (20)	9 (25,7)
Types 1 and 2 FCD / ФКД 1-го и 2-го типов	2 (66,7)	4 (30,7)	3 (27,3)	1 (20)	6 (17,1)
Type 3 FCD / ФКД 3-го типа	1 (33,3)	0 (0,0)	0 (0,0)	1 (20)	4 (11,4)
Cystic gliosis / Кистозно-глиозные изменения	0 (0,0)	5 (38,5)	0 (0,0)	0 (0,0)	8 (22,9)
Polymicrogyria / Полимикрогирия	0 (0,0)	0 (0,0)	1 (9,1)	1 (20)	3 (8,6)
Encephalocele / Энцефалоцеле	0 (0,0)	2 (15,4)	0 (0,0)	0 (0,0)	3 (8,6)
Glioneuronal tumor / Глионейрональная опухоль	0 (0,0)	0 (0,0)	1 (9,1)	1 (20)	2 (5,7)

Note. *FCD – focal cortical dysplasia.*

Примечание. *ФКД – фокальная кортикальная дисплазия.*

section of epileptogenic focus (probably due to the lack of clear boundaries of epileptogenic zone or its location near the functional zone), most of such operations (36.8%) led to a reduction in seizure frequency by at least 75% also observed after tailored resections within more than one lobe (e.g., tailored resection in the parieto-occipital or parieto-temporal region) in 50% of cases, as well as temporal lobectomy (53.1%) and temporal lobectomy combined with tailored resection on another lobe within one brain hemisphere (60%) and all disconnection operations (**Table 9**).

Epilepsy duration

Patients with a shorter length of the disease were more likely to experience lower frequency of seizures by at least 75% (75% percent each in groups with a disease duration shorter than 5 years and from 5 to 10 years long). For the remaining classes, no relation on disease duration was observed (**Table 10**).

Assessing potential predictors of QoL changes / Оценка потенциальных предикторов изменения КЖ

The calculation of Pearson's χ^2 criterion for potential predictors of QoL changes after surgical treatment of epilepsy in incomplete remission shows that statistically significant criteria are presented by seizure frequency and severity ($p<0.001$) (**Table 11**). Most of the parameters considered have no statistical significance with regard to QoL post-surgery in DRE patients ($p>0.05$).

According to the binomial logistic regression analysis, frequency of post-surgery seizures was the only statistically significant factor ($p<0.001$) (**Table 12**).

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Table 9. Correlation between seizures number post-surgery and extent of resection (n=67), n (%)

Таблица 9. Соотношение количества приступов после операции и объема резекции (n=67), n (%)

Extent of resection / Объем резекции	Seizure number post-surgery / Количество приступов после операции					
	More frequent (class I) / Учащение (класс I) (n=3)	Unchanged (class II) / Без изменений (класс II) (n=13)	Reduced by 25–50% (class III) / Сокращение на 25–50% (класс III) (n=11)	Reduced by 50–75% (class IV) / Сокращение на 50–75% (класс IV) (n=5)	Reduced by >75% (class V) / Сокращение на >75% (класс V) (n=35)	Total / Всего
Tailored unilobular / Тейлорированная в пределах 1 доли	3 (15,8)	5 (26,4)	2 (10,5)	2 (10,5%)	7 (36,8%)	19 (100)
Tailored multilobular / Тейлорированная >1 доли	0 (0,0)	2 (33,3)	1 (16,7)	0 (0,0)	3 (50,0)	6 (100)
Temporal lobectomy / Височная лобэктомия	0 (0,0)	5 (15,6)	7 (21,9)	3 (9,4)	17 (53,1)	32 (100)
Temporal lobectomy + tailored multilobular unihemispheric / Височная лобэктомия + тейлорированная в пределах 1 полушария	0 (0,0)	1 (20,0)	1 (20,0)	0 (0,0)	3 (60,0)	5 (100)
Disconnection / Дисконнекция	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	5 (100%)	5 (100)

Table 10. Correlation between seizures number post-surgery and epilepsy duration (n=67), n (%)

Таблица 10. Соотношение количества приступов после операции и длительности заболевания (n=67), n (%)

Epilepsy duration / Длительность заболевания	Seizure number post-surgery / Количество приступов после операции					
	More frequent (class I) / Учащение (класс I) (n=3)	Unchanged (class II) / Без изменений (класс II) (n=13)	Reduced by 25–50% (class III) / Сокращение на 25–50% (класс III) (n=11)	Reduced by 50–75% (class IV) / Сокращение на 50–75% (класс IV) (n=5)	Reduced by >75% (class V) / Сокращение на >75% (класс V) (n=35)	Total / Всего
<5 years/ <5 лет	0 (0,0)	0 (0,0)	1 (25,0)	0 (0,0)	3 (75,0)	4 (100)
5–9 years / 5–9 лет	0 (0,0)	1 (12,5)	1 (12,5)	0 (0,0)	6 (75,0)	8 (100)
10–19 years / 10–19 лет	3 (15,8)	1 (5,3)	2 (10,5)	0 (0,0)	13 (68,5)	19 (100)
≥20 years / ≥20 лет	0 (0,0)	11 (30,6)	7 (19,4)	5 (13,9)	13 (36,1)	36 (100)

Table 11. Pearson χ^2 calculation for the examined potential predictors affecting quality of life in epilepsy patients post-surgery

Таблица 11. Расчет критерия χ^2 Пирсона для каждого из рассмотренных потенциальных предикторов изменения качества жизни после хирургического вмешательства у больных эпилепсией

Parameter / Параметр	p-value / Значение p
Seizure frequency / Частота приступов	**<0,001***
Seizure severity / Тяжесть приступов	**<0,001***
Hemisphere dominance / Доминантность полушария	0,389
Pre-surgery seizure type / Тип приступов до операции	0,548
Neurological deficit / Неврологический дефицит	0,718
Area of surgical intervention / Область оперативного вмешательства	0,417
Epileptogenic substrate morphology / Морфология эпилептогенного субстрата	0,253
Resection extent / Объем резекции	0,215
Epilepsy duration / Длительность эпилепсии	0,062
MRI changes detected / Наличие изменений на МРТ	0,134

Note. *MRI – magnetic resonance imaging.* * *Statistically significant values are highlighted.*

Примечание. *МРТ – магнитно-резонансная томография.* * *Выделены статистически значимые показатели.*

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Table 12. Probability of pre-, peri- and post-surgery factor impact on quality of life in epilepsy patients assessed by binomial logistic regression*

Таблица 12. Определение вероятности влияния до-, пери- и послеоперационных факторов на качество жизни больных эпилепсией методом биноминальной логистической регрессии*

Predictor / Предиктор	Weight / Вес	SE	Z	p
Constant / Константа	–9,9742	3,679	–2,71	0,007
Seizure frequency / Частота приступов	1,8405	0,490	3,756	**<0,001****
Seizure severity / Тяжесть приступов	0,7906	0,850	0,930	0,352
Hemisphere dominance / Доминантность полушария	0,4716	0,821	0,574	0,566
Pre-surgery seizure type / Тип приступов до операции	–0,2784	1,087	–0,256	0,798
Neurological deficit / Неврологический дефицит	–1,5437	1,537	–1,004	0,315
Area of surgical intervention / Область оперативного вмешательства	0,1212	0,244	0,498	0,619
Epileptogenic substrate morphology / Морфология эпилептогенного субстрата	–0,0517	0,229	–0,226	0,821
Resection extent / Объем резекции	0,1307	0,385	0,339	0,734
Epilepsy duration / Длительность эпилепсии	0,3720	0,462	0,804	0,421
MRI changes detected / Наличие изменений на МРТ	2,3146	1,802	1,284	0,199

Note. *SE – standard error; MRI – magnetic resonance imaging. * Model coefficients – improved / not improved. ** A statistically significant value is highlighted.*

Примечание. *SE (англ. standard error) – стандартная ошибка; МРТ – магнитно-резонансная томография. * Коэффициенты модели – стало лучше / не стало лучше. ** Выделен статистически значимый показатель.*

DISCUSSION / ОБСУЖДЕНИЕ

The difficulties while analyzing the outcomes of surgical treatment of epilepsy are often associated with the diversity of patients selected for surgery, the surgical techniques used, and the length of follow-up. The Engel scale is used to assess the frequency of seizures after surgical treatment, and most studies evidence about high correlation between QoL and the absence of epileptic seizures post-surgery [3, 5, 10–13]. Surgery significantly improves patient's QoL in case of complete or near complete seizure elimination.

The data presented in our work show a relatively high level of positive subjective assessment of patients' condition who failed to achieve complete seizure remission (Engel II–IV) after DRE surgical treatment (52.2%), whereas 59.7% of patients had seizure frequency reduced by at least 50%.

The recurrence of epileptic seizures post-surgery is associated with the fact that the areas of rapid seizure spread not included in the resection protocol, acquire epileptogenic potential. This mechanism of adverse outcome implies that the cause of resistance to therapy is more likely to be a widespread epileptic network than a single epileptic focus. Understanding that the epileptic network rather than a single focus undergoes a therapeutic intervention, can change the surgical approach to treatment of focal epilepsy, as well as provide guidance while installing depth electrodes in patients requiring stereo EEG [15].

Among the most frequently identified factors negatively affecting the outcome of surgical treatment are MR negativity, the presence of patient generalized seizures before surgery, the need for diagnostic invasive monitoring [11, 15, 16], as well as multi-focus, bilateral temporal lobes involvement in the epileptic process, and a form of epilepsy affecting the temporal lobe and a unihemispheric part of the brain outside it [17]. Some studies reveal no significant difference in the effectiveness of surgery for temporal and extratemporal localization of epileptogenic zone, because temporal resection provides better outcomes in the first years after surgical treatment, but its effectiveness decreases over the years and the percentage of effectiveness overlaps [18].

MR-positive patients prevailed in our study (92.5%), of which 9 (13.4%) showed changes on both sides. The majority of operations were performed on the temporal lobe (53.7%), as well as resections beyond one lobe of the brain, both tailored and disconnection operations (23.9%). Given the prevalence of MR-positive cases, additional pre-surgical examination was rarely used, PET with 18F-fluorodeoxyglucose was performed in 7.5% of patients, and SPECT according to the SISCOM protocol was also used in 7.5% cases. Each of such studies has own characteristics and limitations, not allowing to apply them in a large number of cases. Invasive video-EEG monitoring was performed only in 26.9% of patients with negative surgery outcomes. Based on these data, it is difficult to assess a correlation between a need for invasive monitoring and outcome of surgery, however, the experience gained may evidence in favor of its use to more accurately locate epileptogenic zone. It is impossible to overestimate this technique while searching for epileptogenic zone in MR-negative forms of focal DRE.

All 3 cases of increased seizure frequency after surgical treatment were noted due to tailored resection of epileptogenic focus, however, most of such operations led to reduced number of seizures (in 47.3% of patients it decreased by more than 50%, of which 36.8% had seizures reduced by at least 75%). In general, this type of surgery was less likely than others to reduce number of seizures, whereas temporal lobectomy, a combination of temporal lobectomy with tailored resection within one hemisphere, and disconnection

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operations led to reduced number of seizures by at least 75% in 53.1%, 60%, and 100% of patients, respectively. In most cases, the failure of tailored resections is associated with the lack of clear epileptogenic zone boundaries or its location near a functionally significant zone.

The majority of patients in our study (73.1%) had a history of combined focal and bilateral tonic-clonic seizures, while a decreased number and severity of seizures was noted in comparable proportions.

Among the morphological features of epileptogenic substrates, hippocampal sclerosis and cystic-gliotic changes correlated with a lower follow-up seizure frequency after surgical treatment, and operations for FCD more often led to unsatisfactory results.

Patients with epilepsy often have comorbid mental issues such as depression, anxiety, and post-seizure psychotic states, which also affect QoL [18], including potential emergence of changes post-surgery. Despite the availability of QoL assessment questionnaires and scales for patients with epilepsy [19], their use is often complicated due to the difficulty of communicating with patients with a negative outcome after surgical treatment. Presumably, this is due to high expectations from surgery and a wish to get rid of disturbing conditions [13, 15], despite detailed epileptologist and neurosurgeon explanations about all potential risks and possible complications after surgical procedures. The percentage of complications after surgical treatment is estimated as high as about 7.9% in temporal and 8.2% at extratemporal lobe epilepsy, respectively, whereas the frequency of persistent neurologic deficit, according to the meta-analysis of patients operated in the period from 2009 to 2019, ranges from 4.1 to 4.4% [20].

Given the resistance to conservative therapy in epilepsy patients undergoing surgical treatment, its effect on the disease course in patients with Engel II–IV outcomes in the current study can be compared with the effectiveness of VNS: according to our data, a reduction in the number of seizures by at least 50% found in 59.7% of patients is comparable to that of VNS therapy, which is evaluated in 22-74.3% of patients with decreased frequency of seizures by at least 50% [21–23]. In addition, neurostimulation therapy exerts several side effects, such as hoarseness of voice, hypersalivation, cough, snoring, cramps and soreness in the neck [21, 23].

Numerous studies draw attention to the impressive length of epilepsy history in patients who were first referred for pre-surgical diagnosis. On average, a patient is prescribed neurosurgical treatment 20 years after the onset of epileptic seizures [24, 25], which is often too late to reverse the psychological, social and comorbid consequences. The average duration of the disease from onset to surgery in our study comprised 19.9 years (from 3 to 43 years). Early surgical intervention for properly selected patients with focal DRE provides a better chance of avoiding lifelong disability and reduces a risk of premature death [25].

Limitations of the study / Ограничения исследования

Among the limitations of the study, it is possible to highlight the small sample size and assessment of patients with unfavorable surgical treatment outcomes separately from the general outcome statistics, which complicates statistical analysis of the presented cohort. In addition, the study may be biased because it includes analysis of patients' own condition assessment and considers the burden of seizures as the main parameter, because the use of specialized tests is irrelevant due to potential neuropsychological abnormalities in patients with any outcome of surgical treatment. It should also be noted that a percentage scale for ratio of seizures number before and after surgical treatment was used, which complicates comparison of the current results with those published elsewhere, but provides a better assessed course of the disease.

CONCLUSION / ЗАКЛЮЧЕНИЕ

Even in case of incomplete success, epilepsy surgery can reduce the number of seizures and improve patients' QoL, but the issue of incomplete seizure remission requires to be further investigated assessing risk analysis, potential complications and adverse events. The only factor significantly affecting QoL in patients with incomplete DRE remission after surgical treatment was found to the frequency of epileptic seizures post-surgery.

ARTICLE INFORMATION	ИНФОРМАЦИЯ О СТАТЬЕ
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Patient consent	Согласие пациентов
All study participants signed an informed voluntary consent	Все участники исследования подписали информированное добровольное согласие
Ethics declarations	**Этические аспекты**
The study was conducted in compliance Helsinki Declaration of the World Medical Association and approved by the Local Ethics Committee of Pirogov National Medical and Surgical Center (session protocol No. 5 dated May 19, 2024)	Исследование проведено с соблюдением принципов Хельсинской декларации Всемирной медицинской ассоциации и одобрено локальным этическим комитетом ФГБУ «Национальный медико-хирургический центр им. Н.И. Пирогова» Минздрава России (протокол заседания ЛЭК № 5 от 19.05.2024)
Data sharing	**Раскрытие данных**
Raw data could be provided upon reasonable request to the corresponding author	Первичные данные могут быть предоставлены по обоснованному запросу автору, отвечающему за корреспонденцию
Publisher's note	**Комментарий издателя**
The statements, opinions, and data contained in this publication were generated by the authors and not by IRBIS Publishing (IRBIS LLC). IRBIS LLC disclaims any responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred in the content	Содержащиеся в этой публикации утверждения, мнения и данные были созданы ее авторами, а не издательством ИРБИС (ООО «ИРБИС»). Издательство снимает с себя ответственность за любой ущерб, нанесенный людям или имуществу в результате использования любых идей, методов, инструкций или препаратов, упомянутых в публикации
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