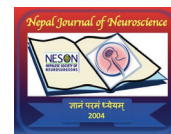


# Age of readiness for epilepsy surgery

Galina Odinstova<sup>1</sup> , Nina Dengina<sup>2</sup> <sup>1,2</sup>Polenov Neurosurgical Research Institute, Branch of Almazov National Medical Research Centre, St. Petersburg, RussiaDate of submission: 18<sup>th</sup> May 2022Date of Acceptance: 14<sup>th</sup> November 2022Date of Publication: 30<sup>th</sup> January 2023

## Abstract

**Introduction:** The average time between epilepsy onset and epilepsy surgery is currently approximately 20 years. In epilepsy, research on the problem of late referral for neurosurgical treatment is crucial.

We aimed to investigate gender differences in the willingness of patients to undergo epilepsy surgery for focal drug-resistant epilepsy (DRE).

**Methods:** It was a single-centre retrospective, observational, longitudinal cohort study in the outpatient and functional neurosurgery departments. We developed a structured questionnaire to examine patients' demographic data, disease history, and perceptions of neurosurgical treatment (duration of epilepsy and optimal age for neurosurgery) in two gender groups. We examined data from 53 patients; eight people were dropped out from the research.

**Results:** Ninety-four point three per cent of outpatients and inpatients answered in the affirmative form the question about their willingness to undergo epilepsy surgery for focal DRE. There were 26 men in group one and 19 women in group two. The disease had been present for  $19.26 \pm 1.35$  years before epilepsy surgery or the decision to undergo surgery. Patients with no significant gender differences between groups considered that the ideal age for neurosurgery was  $18.66 \pm 1.3$  years and that the optimal duration of the disease was  $6.94 \pm 1.02$  years, which was two point eight times shorter than the actual duration of epilepsy.

**Conclusions:** No gender differences in willingness to undergo surgical management of focal DRE were found. The subjective time in which a patient decides to undergo epilepsy surgery is much shorter than the objective time from epilepsy onset to neurosurgery. This could be one of the solutions to the problem of late referral for epilepsy surgery.

**Key words:** Drug-resistant epilepsy, Neurosurgery, Epilepsy onset, Optimal duration, Questionnaire, Willingness

## Introduction

In 2019, the World Health Organization (WHO) published the report "Epilepsy is a Public Health Imperative", which outlines the global social and economic burden of epilepsy.<sup>1</sup> There are currently more than 65 million people with epilepsy worldwide.<sup>2</sup> Despite

recent updates in epilepsy classifications, seizures, and the definition of drug-resistant epilepsy (DRE), the issue of epilepsy management remains a hot topic.<sup>3-4</sup> Common and new antiepileptic drugs (AEDs) can achieve regression of clinical and electroencephalographic (EEG) manifestations of epilepsy in 60 to 70% of cases.<sup>5</sup> In 2010, the International League Against Epilepsy (ILAE) defined DRE as the non-response of patient's seizures to at least two antiepileptic drugs appropriately selected and taken over a relevant period of time<sup>4</sup>. When focal DRE develops, the chance of achieving seizure control with medication is less than eight percent, whereas neurosurgery can achieve complete seizure control in an average of 68% of patients.<sup>6</sup> The effectiveness of additional drug treatment decreases over time as the disease progresses. In adults, the average time between epilepsy diagnosis and surgery is currently approximately 20 years.<sup>7</sup> Uncontrolled seizures have negative social and economic consequences for patients and society.<sup>8</sup> Both the perspective of clinicians and patients influences the planning of surgery.<sup>9</sup> Patients are often assumed to be subjectively unprepared for epilepsy surgery.<sup>10</sup> However, little research has been done on patients' subjective readiness to undergo epilepsy surgery. Therefore, the process of finding solutions to the problem of late referral for neurosurgery in epilepsy is of importance. Of particular interest is the opinion of a specific group of

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### Address for correspondence:

Odinstova Galina V.

Polenov Neurosurgical Research Institute, 12 Mayakovskogo Str., St. Petersburg, 191014, Russia

Mobile number: +7-911-218-78-36

E-mail: [odinstova\\_gv@almazocentre.ru](mailto:odinstova_gv@almazocentre.ru)

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patients - patients in a neurosurgical department who are considering neurosurgical management for epilepsy.

The purpose of this study was to find out if there are gender differences in patients' willingness to undergo epilepsy surgery for focal DRE.

## Material and methods

We conducted this study in 2019-2020 at Polenov Neurosurgical Institute in Saint Petersburg, Russia. The present study is part of a prospective observational study commissioned by the government of the Ministry of Health of the Russian Federation (Topic No. 056-00119-22-00 'Risk stratification, selection of optimal surgical treatment strategy and prediction of outcomes in patients with drug-resistant structural epilepsy'). It was a single-centre, retrospective, observational, longitudinal cohort study in the departments of ambulatory and functional neurosurgery. In this study, we did not consider objective criteria such as medical and socioeconomic factors that influence the duration of the disease before epilepsy surgery. This study is part of a wider project entitled Subjective willingness to undergo epilepsy surgery, which has been previously reported.<sup>11</sup>

### *Selection of patients*

We first reviewed clinical data from 53 patients with DRE between 1 January 2019 and 31 December 2020. Patients who considered surgical methods as part of their DRE management were included in the study.

### *Inclusion criteria*

A patient 1) must sign an informed consent form; 2) must be at least 18 years of age; 3) must have a documented diagnosis of DRE; 4) must have a stable dosage of concomitant AED during the 3-month observation period; 5) in the opinion of the investigator, must be able to understand the questions; 6) in the opinion of the investigator, must be able to complete the questionnaire satisfactorily.

### *Exclusion criteria*

Patients 1) must be unable to provide informed consent; 2) must not be a child; 3) be pregnant; 4) must not be able to understand the questions; 5) must not be able to complete the questionnaire; 6) have refused neurosurgical treatment for personal reasons; 7) have been refused further neurosurgical treatment.

We dropped out eight people from participation in further research. We divided the remaining 45 patients into two groups according to gender: men in group one and women in group two.

### *Survey*

We developed the structured interview questionnaire "Subjective readiness for epilepsy surgery" (Additional file 1). We used it to interview patients. Patients were asked to complete questionnaires with several sections: demographic information, epilepsy history. We included the following questions in the questionnaire: patients' willingness to undergo neurosurgery, acceptable duration of the disease before brain surgery, and the age at which patients believe neurosurgery should be performed. We looked at survey results, cohorts, and group indicators.

### *Standard protocol approvals, registrations, and patient consents*

Each research participant was provided with all essential information. This study was approved by the Ethics Committee of Almazov National Medical Research Centre (20 May 2020, reference number: 29/XI-7), and informed consent was signed by all participants.

### *Statistical analysis*

We used Fisher's exact test for a contingency table to calculate the p-values of the clinical information. Comparisons of medians were made using the Mann-Whitney U test. Statistical significance was set at  $p < .05$ . We used StatSoft Statistica (v.8.0) to estimate the data from our study.

## Results

There are 3 parties involved in the decision to operate: the patient, the neurologist and the neurosurgeon. In recent years, interest in surgical treatments has increased greatly. Surgeons are willing to operate on patients as early as possible. On the part of neurologists, however, the opposite can be observed. Our survey of physicians involved in the treatment of patients with epilepsy found that 78% of neurologists consider surgical management of the disease to be low. However, only 48% think that this method should be expanded. 9% of neurologists consider the method dangerous, 27% find it difficult to answer and only 15% consider the surgical management of epilepsy acceptable. As a result, the method is considered an extreme measure by most neurologists, so they refer patients late for preoperative diagnosis. It turns out that the treating doctors do not inform the patients in time. And in this situation, the opinion of the third party, the patient, was of particular interest.

According to the exclusion criteria, eight patients were excluded from the study. Three of the 53 patients felt that epilepsy surgery would not have been necessary in their cases. When it came to assessing whether surgery would be appropriate in their particular case, the other three people were confused. One patient refused to complete the

questionnaire. As a result of the inclusion of 45 patients, the subjective psychological willingness of the patients to undergo epilepsy surgery was 94.3%.

*Demographic data*

Consequently, group one was composed of 26 men (58%) and group two included 19 women (42%). The ratio of men to women was 1.4: 1. (Fig.1)

The mean age of the cohort was 30.96 ±1.07 years. There were no statistically significant age differences between the two groups. At the time of the study, the average age of the women was in the late reproductive phase of their lives (Table 1).

*Table 1: Indicator of age.*

indicators	Group 1	Group 2	The cohort
mean (in years)	30.92±1.23	31±1.95	30.96±1.07
median (in years)	31,5	31	31
mode (in years)	28	31	28
minimum (in years)	18	20	18
maximum (in years)	49	54	54

*Epilepsy anamnesis*

The average duration of epilepsy before brain surgery was 19.26±1.35 years, reflecting a general problem of late epilepsy surgery. The average age at the first unprovoked seizure was 11.69±0.96 years, suggesting childhood epilepsy. The differences between the groups in gender, duration of epilepsy, and age at onset were not statistically insignificant. Consequently, the duration of epilepsy did not differ between the gender groups.

All patients had uncontrollable seizures. The average frequency of seizures was 4 seizures per month. The frequency of seizures ranged from two to 20 seizures per month. Generalized seizures occurred more frequently

than focal seizures. Polymorphic seizures affected the vast majority of patients. All patients had the last seizure in the current month.

*Survey results*

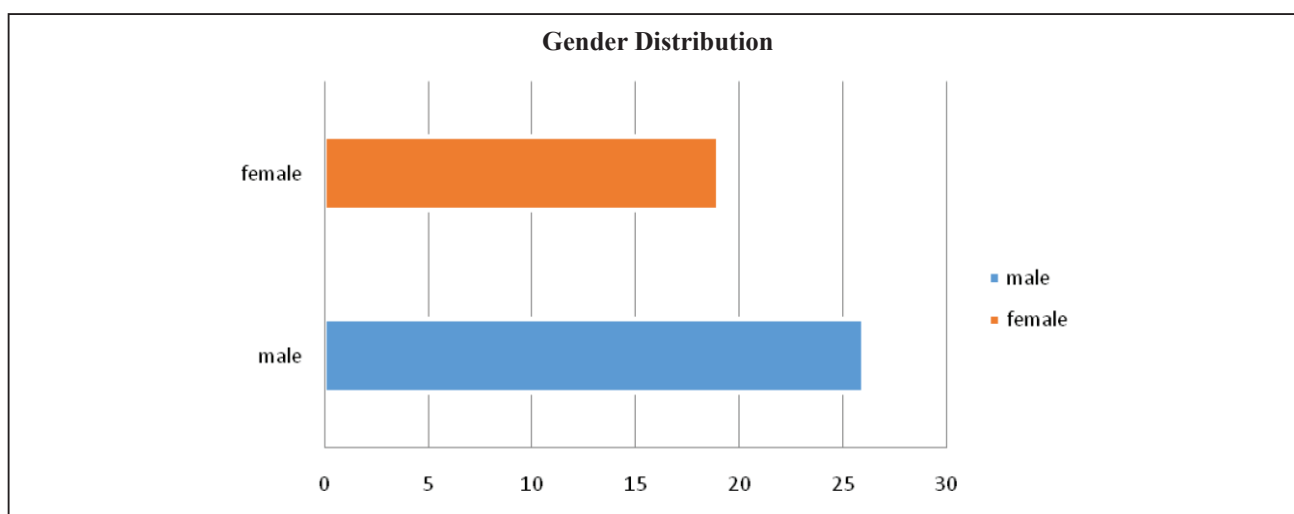
Subjective indicators of willingness to undergo epilepsy surgery were compared with real values for age and duration of the disease. All patients agreed that the best age for neurosurgery was 18.66±1.3 years and the optimal duration of the disease was 6.94±1.02 years. (Fig. 2).

Regarding the proper age for epilepsy surgery, we did not find significant differences between the groups.

In both groups, this age represented the beginning of the transition to the adult network. It was due to the ability to make their own decisions independently of the parents' opinion. Epilepsy surgery was performed at an age one to seven years above the optimal age. The responses of the patients indicated that the ideal duration of the disease before epilepsy surgery (6.94±1.02 years) was significantly less than the actual duration of disease (19.26±1.35 years), determined by the Wilcoxon signed-rank test ( $z = -5.305, p < 0.001$ ).

With no statistically significant differences between the groups, the ideal duration of the disease was two point eight tenths times shorter than the actual duration. It should be noted that at the time of the diagnosis of epilepsy, 12 patients (27%) preferred neurosurgical management, which contradicts the established criteria for focal DRE and is not an indication for surgery or a reason for epilepsy surgery. Among those who favoured immediate surgery, there was a clear gender imbalance: four out of 26 (15,4%) men and eight out of 19 (42%) women preferred it.

Thus, reducing the duration of epilepsy before neurosurgical treatment through subjective willingness of patients is a modifiable factor to address the problem of late referral to neurosurgery.



*Figure 1: Distribution of gender within the cohort.*

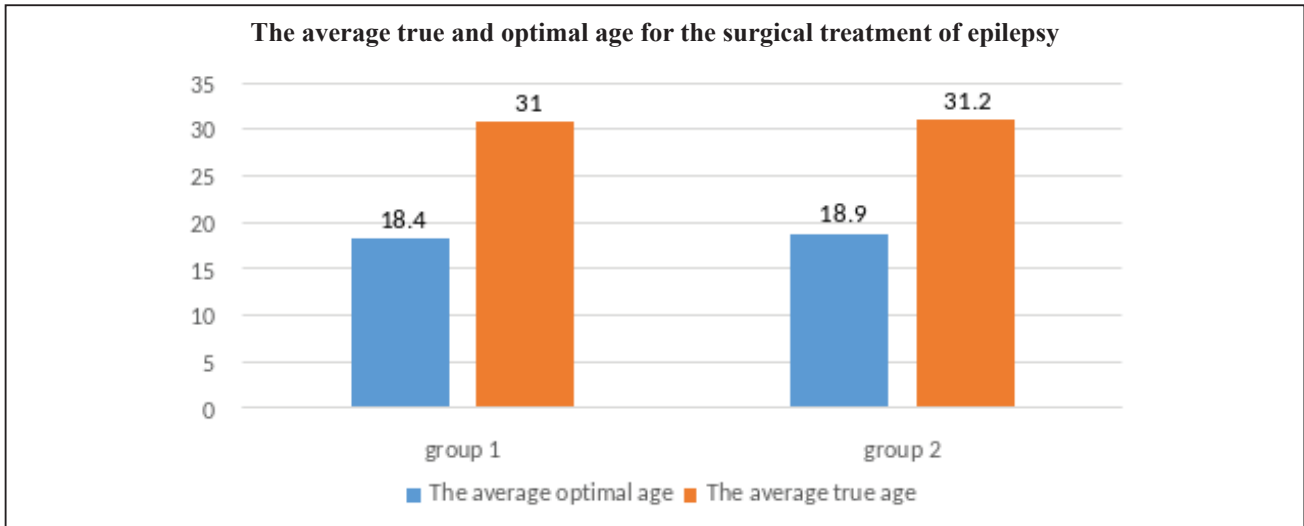


Figure 2: The true and optimal average age for epilepsy surgery.

## Discussion

Thus, the results of the study confirm that patients with epilepsy were well prepared to accept epilepsy surgery before being selected for neurosurgery. However, patients are usually referred for surgery only after 20 years of seizures, which is often too late to prevent significant disability and premature death.<sup>12</sup> As a result of a long period of uncontrolled seizures, status epilepticus is becoming more common. It is also worth noting that status epilepticus is one of the most dangerous complications of the disease.<sup>13</sup> At the same time, neurosurgical treatment of focal long-term DRE can be effective and safe, with a common side effect, postoperative memory loss, having minimal impact on daily life.<sup>14</sup> These results contradict the commonly accepted notion that epilepsy patients are emotionally unprepared for neurosurgical management. However, the desire of more than a quarter of patients to “have surgery immediately” indicates that patients are unaware of or misunderstand the basic goal of epilepsy therapy, leading to neurosurgery only beginning after a diagnosis of DRE. As a result, the duration of epilepsy before brain surgery is a controllable indicator. The development of novel neurosurgical and therapeutic approaches to epilepsy has the potential to reduce the time required for neurosurgical treatment.<sup>15</sup> Raising awareness of potential neurosurgical methods among physicians, healthcare professionals, and patients is a promising way to reduce the number of patients suffering from uncontrolled seizures.<sup>16</sup>

## Conclusions

There were no gender differences in willingness to undergo surgical management of focal DRE. The

subjective time in which a patient decides to undergo epilepsy surgery is much shorter than the objective time from epilepsy onset to epilepsy surgery. This could be one of the solutions to the problem of late referral for epilepsy surgery.

## Abbreviations

**DRE:** drug-resistant epilepsy

**EEG:** electroencephalographic

**ILAE:** The International League Against Epilepsy

**AED:** antiepileptic drugs

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## Competing interests

The authors declare that they have no competing interests.

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