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# Seizure outcomes after hemispherectomy for drug resistant epilepsy in childhood and adolescence

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ABSTRACT

*Objective and purpose:* Hemispherectomy produces remarkable results in terms of seizure outcomes and quality of life for drug resistant hemispheric epilepsy. We reviewed the neurophysiology, neuroradiologic findings, pathologic findings, epilepsy characteristics, and clinical long-term outcomes in childhood and adolescence patients following a hemispherectomy. This study explores the post hemispherectomy seizure outcomes.

*Methods:* We retrospectively reviewed the records of 64 patients after a hemispherectomy at King faisal Specialist Hospital and Research Center between 2000 and 2014. Clinical, EEG, imaging, and surgical data were collected. Seizure outcome evaluated during follow-up in 1, 3, and 5 years.

This study was approved by the ethics committee in King Faisal Specialty Hospital and Research Center (RAC# 2161 142).

Patient consent to review their medical records was not required by the institutional Office of Research Affairs of the King Faisal Specialty Hospital and Research Center because this is a retrospective study. Patient confidentiality was ensured because patient identity not reported and no single information about patient names or info.

*Results:* Our cohort consisted of 26 male and 38 female children and adolescents. The majority of seizure onset during neonatal period, and the youngest age at surgery was 4 months old. Seizure frequency recorded at home as daily in 36 patients (56.25%), with significant impacts on their life.

Focal cortical dysplasia (FCD) confirmed in a total of 17 cases (26.56%), leptomeningeal angiomatosis (sturge-weber syndrome) 2cases (3.13%), Heterotopia in 10 cases (15.63%), Gliosis in 13 cases (20.31%), Sclerosis 4 cases (6.25%), Chronic inflammation 6 cases (9.38%), Encephalomalacia 8 cases (12.5%) Brain tumors 3 cases (4.68%). Single cases of sole Cavernous angioma were diagnosed.

In our study, most of the children and adolescents achieved seizure freedom. At follow up of 1–5 years, after first year follow up 39 patients (67.24%) achieved seizure freedom (ILAE I), and Three years follow-up after hemispherectomy, revealed 23 patients (59%) achieved seizure freedom (ILAE I) While five years follow up of hemispherectomy patients showed (ILAE I) in 7 patients (44%).

*Conclusions:* This study shows good long-term seizure outcomes after hemispherectomy. Seizure freedom has been achieved in the majority of the patients after 3 and 5 years.

## 1. Introduction

Hemispherectomy was introduced by Walter Dandy in 1928 for removal of a right hemispheric glioma, but was pioneered for use in catastrophic epilepsy by McKenzie a decade later.

Hemispherectomy is now a well-established procedure for holohemispheric drug-resistant epilepsies, constituting 20–40% of all pediatric epilepsy surgeries at some centers [1].

These epilepsies are often associated with hemimegalencephaly, porencephaly, and malformations of cortical development, Sturge–Weber syndrome, infantile hemiplegia, and Rasmussen's encephalitis. Other etiologies that may be appropriate for hemispherectomy include stroke, trauma, arteriovenous malformations, hemiatrophy, and tuberous sclerosis [1].

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Seizure reduction rates after hemispherectomy have ranged between 50% and 92%, however, this study's lie in its large sample size of 64 subjects and in the duration of 5 years follow-up.

Generally, early intervention in pediatric has been recommended in multiple studies to address both the seizure burden and the developmental delay [2].

Candidates for hemispherectomy typically have hemiparesis and other baseline neurologic deficits that lateralize to the epileptic hemisphere. Furthermore, due to its overall long-term cognitive, behavioral, and psychosocial benefits, this surgery is also recommended in individuals who have retained some functions in the diseased hemisphere, especially when surgery is performed early [1].

8 patients were identified in our hospital, who had proven paradoxical lateralization of scalp EEG ictal patterns, demonstrated by seizure freedom after epilepsy surgery, data from invasive electroencephalography, or imaging and seizure semiology, helping to correctly lateralize the ictal EEG pattern. The ideal timing of surgery with respect to age at presentation was the goal in most of our patients with refractory epilepsy and predictors of good outcomes as in our study and the consequence of underlying pathology on outcome is only slowly emanate. Anatomical hemispherectomy has after a while become a widely used surgical approach for drug resistant epilepsy secondary to hemispheric pathology such as in Rasmussen encephalitis, Sturge-Weber syndrome, hemimegalencephaly, and hemispheric infarct [3], which was previously our surgeon approach. Although this surgical technique has been correlated with seizure-free rates of 70–80% in previous studies [3]. But because early and delayed surgical complications following this procedure, with associated high mortality rates, functional hemispherectomy was introduced in 1983 by Rasmussen based on a combination of the partial anatomic excision and disconnection of the remaining lobe. Additionally, hemispherotomy incorporating partial cortical removal with less adverse events while still producing excellent results [3].

Our cases of 64 patients who underwent hemispherectomy, with the goal of assessing longitudinal outcome of seizure freedom rates and predictors of seizure outcome.

## 2. Methods

We retrospectively reviewed the patients who underwent hemispherectomy between 2000 and 2014 in kingdom of Saudi Arabia.

The patients were examined for the surgical candidature after failure of medications that made epilepsy to be considered resistant: drug resistant epilepsy was considered when at least three drugs at the optimal and maximal dosage were used without seizure control.

Patients had been assessed using a clinical, radiological, neurophysiological, neuropsychological and neuropsychiatric data. Then, the data were discussed at a multidisciplinary meeting and these reports form the prospective aspect of this study. Each patient was evaluated using MRI, video EEG telemetry, with or without PET Scan.

All patients were assessed in the Epilepsy monitoring Unit in king faisal specialty hospital and research center in Riyadh. Before and after surgery using a standard procedure as follows:

History and clinical examination.

Ictal/Interictal long term scalp video-EEG examination.

Neuroimaging (MRI and PET scan).

Neuropsychological assessment.

(General intelligence and specific abilities)

Evaluation of functional status.

Generally, after surgery this procedure was performed at outcome; in some cases there was a serial assessment.

### 2.1. Seizure evaluations

Epilepsy was classified according to the International League Against Epilepsy (ILAE) classification [4].

This classification system is as follows:

1. Completely seizure free, no auras.
2. Only auras; no other seizures.
3. 3.1–3 seizure days/year; ± auras.
4. Four-seizure days/year to 50% reduction of Baseline seizure days; ± auras.
5. Less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; ± Auras.
6. More than 100% increase of baseline seizure days; ± auras.

Pre-surgery EEG was aimed for seizure evaluation including: type of seizure, localization, extent, frequency of interictal epileptiform discharges in both the affected and healthy hemispheres; the presence of independent, asymmetric or synchronic discharges was also evaluated. Furthermore, ictal patterns were analyzed, with consideration to the focal location of seizure onset and the type of extension.

### 2.2. Neuroimaging

All the patients evaluated from 2011 to 2014 were examined using a 3 T MR system and those evaluated from 2000 to 2010 using a 1.5 Tesla MR system. MRI was repeated after surgery at least once and sometimes the neuroimaging control was performed with a CT scan [5].

## 3. Patients and methods

### 3.1. Patient selection

We retrospectively reviewed the medical records, findings of presurgical evaluation, surgical procedures, and outcomes of 64 children and adolescents who underwent hemispherectomy for medically refractory epilepsy at our Centre, Patients were assessed and followed-up for at least 1 to 5 years after surgery. Six of the patients have been recently reported in the last 9 months of (2014).

Presurgical evaluation was performed including comprehensive medical history, full neurologic examination, long-term scalp video-EEG recordings, high resolution MRI, and psychological assessment.

Preoperative data were reviewed at a multidisciplinary meeting before proceeding to surgery. The decision to proceed to surgery was based on lateralizing EEG or MRI findings, seizure semiology, and neurologic deficit. The indication for surgery was carefully considered against the risk of neurologic deterioration and the general risks of a major neurosurgical procedure.

All resections were performed by different neurosurgeons with different surgical approaches. Etiology was classified as congenital, acquired, or progressive, according to neuroimaging and histopathology findings.

### 3.2. Preoperative EEG findings

The interictal and ictal EEG recordings were reviewed. Interictal EEG was classified according to localization and lateralization of epileptiform discharges. Majority of Ictal onset location over entire one hemisphere 19 Cases (37.25%) Cumulative Percent (92.16%). (Fig. 1).

In addition to major ipsilateral EEG abnormalities, contralateral interictal or ictal EEG abnormalities were established, Ictal EEG was classified as right in 20 cases (31.25%), whereas 26 (40.63%) presented a left lateralization, 5 (7.81%) had generalized epileptic discharges, and 8(13.56%) with different onset in each ictal EEG onset (Table 1), but with one hemisphere predominance However, surgical decision done in all the cases with summation of History, clinical examination, Video EEG “analysis of all seizures semiology “Long term Scalp Or invasive recording of EEG results, MRI brain and PET Scan finding.

Interictal EEG abnormalities also classified according to localization and lateralization of epileptiform discharges. Interictal EEG was

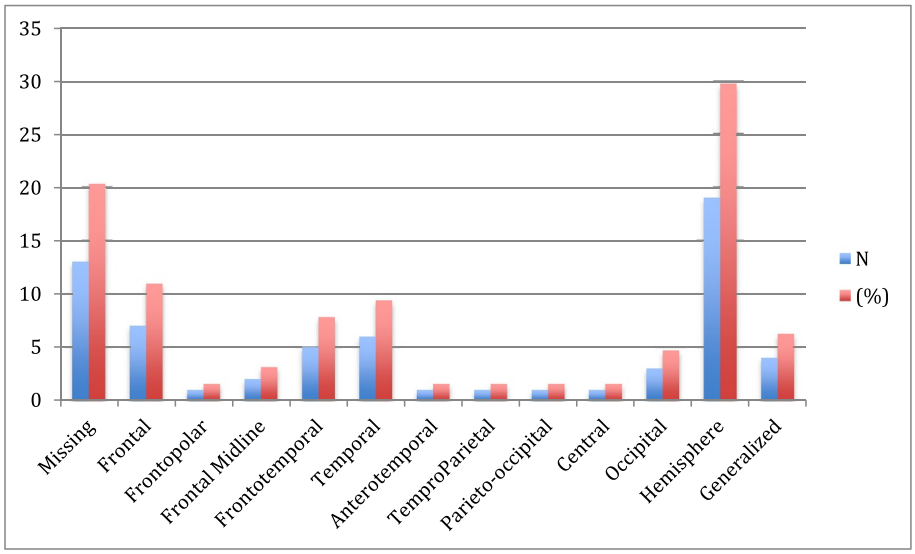


**Fig. 1.** Majority of Ictal onset location over entire one hemisphere (37.25%).

**Table 1**
First Ictal EEG Lateralization.

| First Ictal EEG Lateralization | | | | |
|---|---|---|---|---|
| IEEGLat1 | Frequency | Percent | Cumulative Frequency | Cumulative Percent |
| Missing | 5 | 7.81 | 5 | 7.81 |
| Right | 20 | 31.25 | 25 | 39.06 |
| Left | 26 | 40.63 | 51 | 79.69 |
| Generalized | 5 | 7.81 | 56 | 87.50 |
| Multifocal | 8 | 12.50 | 64 | 100.00 |

classified as right in 18 cases (28.57%) whereas 23 (36.51.%) presented a left EEG lateralization, which is compatible with Ictal EEG lateralization and EEG localization as also majority of Interictal location over entire one hemisphere 25 cases (42.37%).

### 3.3. Preoperative MRI findings

The presurgical MRI 1.5-3 T Magnetom scans of all 64 patients, including T1, T2, and fluid-attenuated inversion recovery (FLAIR) sequences were analyzed retrospectively. Significant MRI findings contralateral to the severe, extensive abnormality identified as the epileptogenic lesion were noted. Contralateral subtle abnormalities such as small single white matter lesions, or subtle T2 hyperintensity noted.

In 62 patients, MRI diagnosis was established, including 15 patients with hemimegalencephaly, 8 with focal cortical dysplasia, 10 with encephalomalacia, one with hemispheric polymicrogyria, 12 with atrophy, and 4 with remote infarction, and majority of MRI abnormalities hemispheric 37 patient (60.66%). Fig. 2.

## 4. Results

### 4.1. Postoperative

#### 4.1.1. Patient selection

Our cohort consisted of 26 male and 38 female children and adolescents.

The majority of seizure onset during neonatal period, and the youngest age at surgery was 4 months old. (Figs. 3 and 4).

Seizure frequency recorded at home as daily in 36 patients (56.25%), with significant impacts on their life.

Histopathology confirmed focal cortical dysplasia (FCD) in a total of 17 cases (26.56%),leptomeningeal angiomatosis (sturge-weber syndrome) 2cases (3.13%), Heterotopia in 10 cases(15.63%), Gliosis in 13 cases(20.31%),Sclerosis 4 cases (6.25%), Chronic inflammation 6 cases (9.38%),Encephalomalacia 8 cases (12.5%) Brain tumors 3 cases (4.68%). Single cases of sole Cavernous angioma were diagnosed.

#### 4.1.2. Surgical procedures and early postoperative course

Of 64 procedures, the earliest surgeries were performed in children with congenital etiology, 14 patients operated in the first year of life, youngest age was 4 months old and epilepsy diagnosis made during the first year of life in 35 patients, 29 of them during neonatal period (Fig. 3).

The postoperative course was uneventful in all patients. In our cohort, there were no perioperative mortalities, despite considerable blood losses. No complication for 35 patients (54.69%)where Late sequelae concerned hydrocephalus, included in 3 patients (4.69%), which required a ventriculoperitoneal shunt at 1–13 months after surgery. Ventricular hemorrhage one patient (1.56%), 'Transient versus permanent' hemiparesis or plegia 7 patients (10.94%) although most of our cases presented with hemiparesis or plegia prior surgery.

### 4.2. Seizure outcomes

Hemispherectomy surgery considered as an efficacious procedure in terms of seizure control and allows consequent discontinuation of antiepileptic drugs in the majority of selected cases.

At follow up of 1–5 years, after first year follow up 39 patients (67.24%) achieved seizure freedom (ILAE I), 1–3 seizures (ILAE III) seen in 2 patients (3.45), and more than 3 seizures 17 patients (29.31%) (ILAE IIII).

Three years follow-up after hemispherectomy, 23 patients (59%) achieved seizure freedom (ILAE I), 2 patients seizure free with aura 5% (ILAE II), 3 patients (8%) (ILAEIII) and more than three seizures in 11 patients (28%) (ILAEIIII).

While five years follow-up of hemispherectomy patients done for the patients continue their follow up with epilepsy clinic and showed (ILAE I) in 7 patients (44%), (ILAE III) in 2 patients (13%) and (ILAE IIII) 7 patients (44%). (Fig. 5).

Following surgery, patients were evaluated at 3, 6, 12, and 24 months and then yearly in the case of seizure freedom or at appropriate intervals in case of seizure recurrence. The numbers of patients drop during follow up as no show. Seizure outcomes were classified according to the ILAE scales.

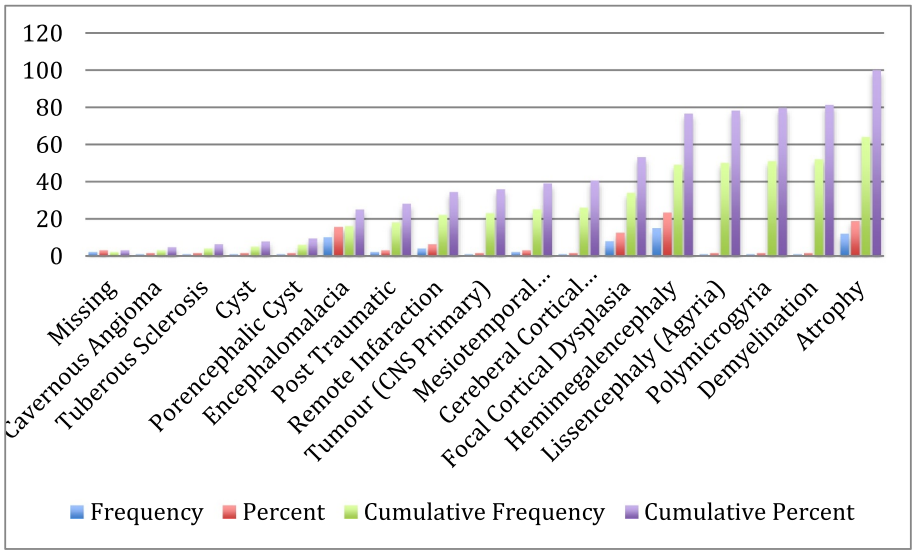


**Fig. 2.** Neuropathological causes of refractory epilepsy showed different etiological groups: Hemimegalencephaly, atrophy and encephalomalacia in majority of patients.

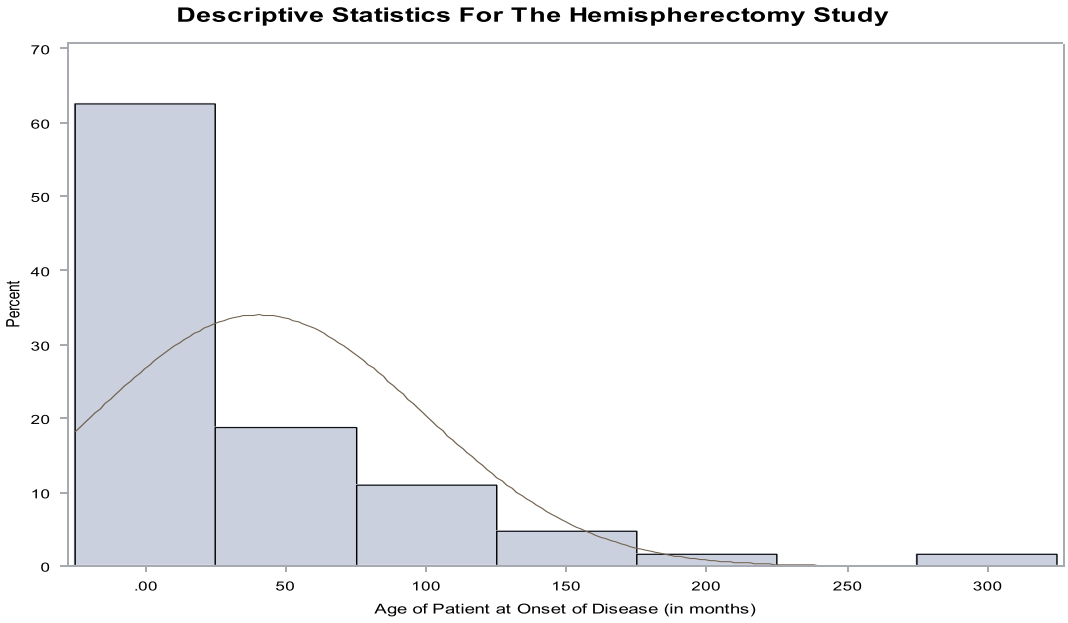


**Fig. 3.** Age of patients at onset of epilepsy: majority at the first year of life.

Postoperative withdrawal of antiepileptic drugs initiated between 1 and 2 years after successful epilepsy surgery, according to patient characteristics and etiology.

In carefully selected children, hemispherectomy results in seizure-free rates of 70–80%. The evidence from durable reports indicates that the benefit of this procedure is maintained over time; 60% remain seizure free after 5 years [6].

## 5. Discussion

In this study, we intended to investigate the seizure outcomes of children and adolescents that underwent hemispherectomy for drug resistant epilepsy at the Epilepsy unit. In this cohort of 64 hemispherectomy patients, the vast majority of selected children and adolescents achieved seizure freedom.

At present, evidence for performing epilepsy surgery in the first years of life is encouraging. Early surgical intervention was shown to be effective with seizure freedom achieved in 48–73% of children operated on before the age of three years in 1979–2007 [7].

While parents generally report a dramatic change in quality of life and social-behavioral skills corresponding to seizure alleviation, this should encourage pediatric epileptologist to consider early surgical intervention in young children and initiate a comprehensive presurgical evaluation [7].

Epilepsy surgery should be integrated in therapeutic regimes at an early stage, in drug resistant epilepsy patients, in order to improve access and prevent treatment delay and to allow the resumption of developmental progression during critical stages of brain Maturation in pediatric patients.

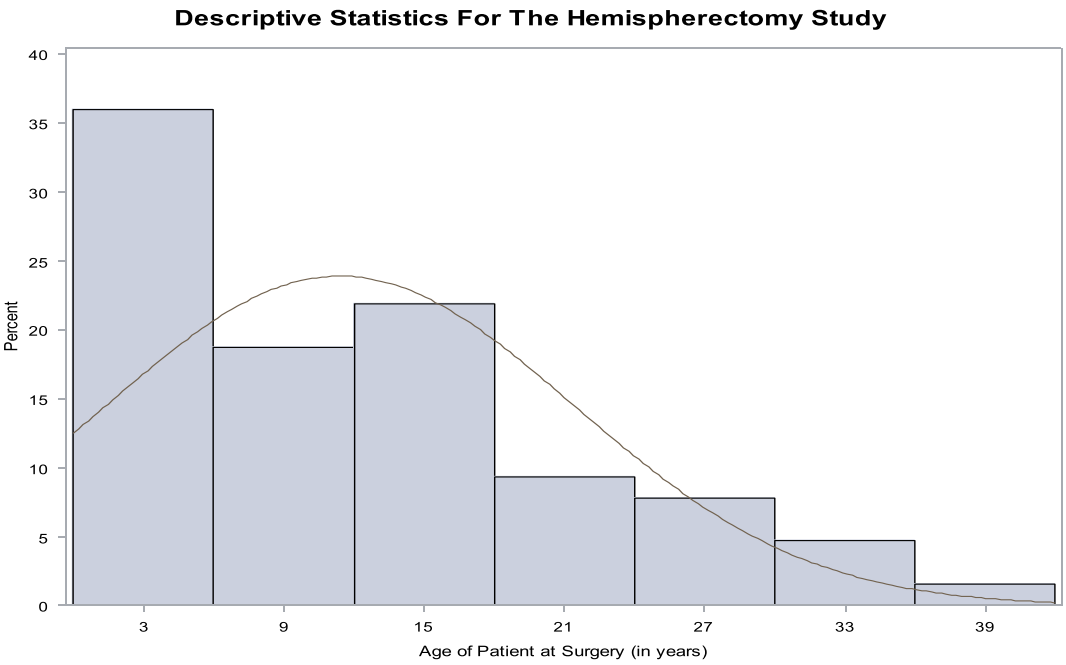


**Fig. 4.** Age of patient at surgery: youngest age operated was 4 months old.

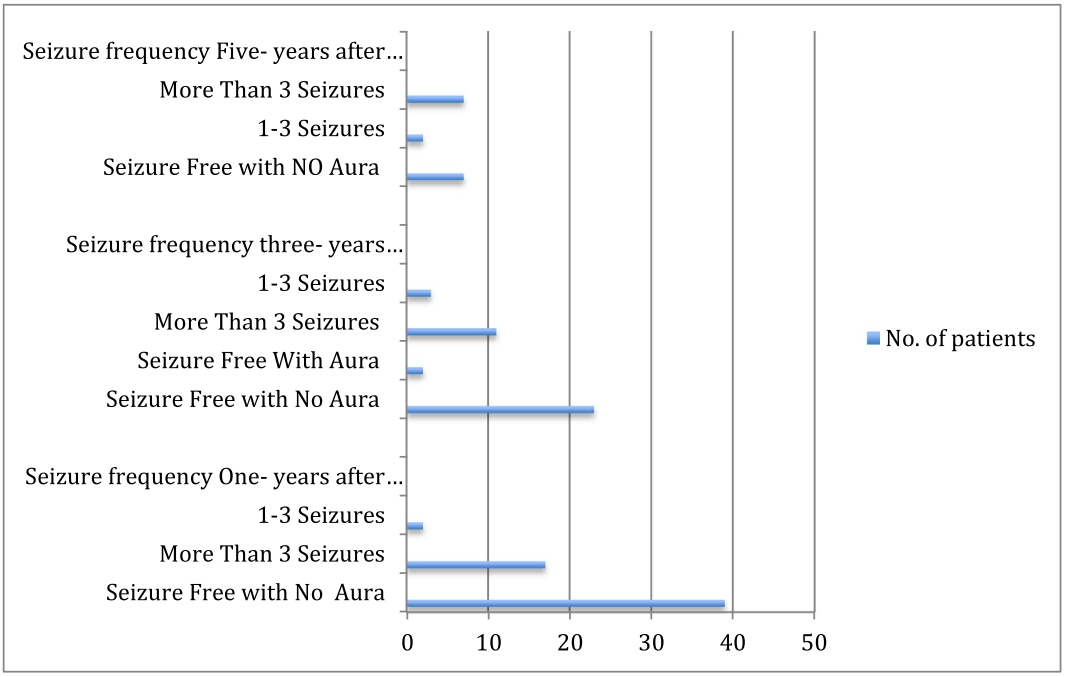


**Fig. 5.** Seizure frequency One, Three and Five- years after surgery following ILAE.

## Declaration of Competing Interest

Noting any conflicts of interest.

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