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# Absolute spike frequency as a predictor of surgical outcome in temporal lobe epilepsy

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ABSTRACT

*Purpose:* Frequent interictal epileptiform abnormalities may correlate with poor prognosis after temporal lobe resection for refractory epilepsy. To date, studies have focused on limited resections such as selective amygdalohippocampectomy and apical temporal lobectomy without hippocampectomy. However, it is unclear whether the frequency of spikes predicts outcome after standard anterior temporal lobectomy.
*Method:* Preoperative scalp video-EEG monitoring data from patients who subsequently underwent anterior temporal lobectomy over a three year period and were followed for at least one year were reviewed for the frequency of interictal epileptiform abnormalities. Surgical outcome for those patients with frequent spikes (>60/h) was compared with those with less frequent spikes. Additionally, spike frequency was evaluated as a continuous variable and correlated with outcome to determine if increased spike frequency correlated with worse outcome, as assessed by modified Engel Class outcome.
*Results:* Forty-seven patients (18 men, 29 women; mean age 40 years at surgery) were included. Forty-six patients had standard anterior temporal lobectomy (24 right, 22 left) and one had a modified left temporal lobectomy. There was no significant difference in seizure outcome between those with frequent (57% Class I) vs. those with less frequent (58% Class I) spikes. Increased spike frequency did not correlate with worse outcome. Greater than 20 complex partial seizures/month and generalized tonic-clonic seizures within one year of surgery correlated with worse outcome.
*Conclusions:* This study suggests that absolute spike frequency does not predict seizure outcome after anterior temporal lobectomy unlike in selective procedures, and should not be used as a prognostic factor in this population.



## 1. Introduction

Anterior temporal lobectomy is the most frequently performed type of epilepsy surgery. Numerous studies have evaluated potential prognostic factors for predicting surgical outcome after temporal lobectomy. Unilateral temporal lobe pathology, including mesial temporal sclerosis, age of first risk <5 years of age, lack of secondarily generalized seizures, unilateral interictal epileptiform discharges, mesial temporal sclerosis on MRI, and PET temporal hypometabolism are favorable predictors of post-operative seizure-freedom ([1–3,5]). In contrast, low IQ, high pre-operative seizure frequency (>20 complex partial seizures per month) as well as the presence of a generalized tonic clonic seizure within one year prior to surgery are poor prognostic factors [4].

Interictal epileptiform abnormalities may also help predict surgical outcome. However, data are conflicting regarding correlation of the state of epileptiform abnormalities and surgical outcome. One study found that the lateralization of spikes in wakefulness and REM sleep more strongly correlate with epilepsy surgery outcome [8]. However, the opposite was seen in another study, with lateralization of spikes in non-REM sleep correlating more strongly with the seizure focus and surgical outcome than those occurring in wakefulness [6].

Recent reports have suggested that absolute interictal spike frequency may also have predictive value. Krendl and Gymiesi both reported that absolute spike frequency (independent of spike distribution) is predictive of postoperative seizure control in patients undergoing primarily selective amygdalohippocampectomy or apical temporal lobectomy without hippocampectomy. It has been hypothesized that since spikes recorded on scalp EEG must spread to involve the neocortex, the frequent spiking may represent an extended irritative zone that may not be resected

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during selective surgery. Therefore, the larger the area that is involved the higher the spike frequency. Another possibility is that there are different subpopulations of patients with TLE and certain groups have a lower baseline spike frequency and seizure frequency and thus a better surgical outcome, unrelated to area of the epileptic focus.

It is not clear if spike frequency is predictive of outcome after anterior temporal lobectomy. Effects of this procedure might not be affected by spike rates, as a larger area is being resected if the increased spike frequency correlates with a larger epileptogenic zone. This study aims to evaluate the prognostic significance of spike frequency in this population. We hypothesize that increased spike frequency is not a poor prognostic factor for surgical outcome in standard temporal lobectomy.

## 2. Methods

Inclusion criteria for the study were as follows: (a) refractory TLE patients who underwent a unilateral standard or selective temporal lobectomy during a three year period, (b) pre-surgical long term video EEG monitoring at Thomas Jefferson University Hospital (TJUH) for at least five days, (c) MRI brain for first time epilepsy surgery, and (d) minimum postoperative follow-up of 1 year. Study patients were evaluated by continuous scalp video EEG monitoring using the Standard International 10-20 System with anterior temporal or sphenoidal electrodes.

Patients who did not undergo epilepsy surgery or patients lost to follow up before 1 year were excluded, as well as patients who underwent multilobar resections, corpus callosotomies, or multiple subpial transections. Anterior temporal lobectomy was performed as described previously and typically consisted of 4–4.5 cm resection measured laterally from the anterior temporal tip for dominant resections and 5–5.5 cm lateral resection for non-dominant resections, though the extent of lateral resection, especially superiorly has diminished in recent years, to 2–2.5 cm in the dominant hemisphere and 3–3.5 cm in the non-dominant hemisphere.

Data collection also included a surgical database and medical chart review to obtain the history for other variables which may affect outcome, including age at seizure onset, duration of epilepsy, seizure type and frequency and epilepsy risk factors such as head trauma, a family history of epilepsy, and history of febrile seizures.

MRI brain interpretation as determined by independent review of the MRI by a board certified neuroradiologist at the time of surgical conference was used to determine the presence or absence of mesial temporal sclerosis (MTS) or any other focal lesions.

Absolute spike frequency was assessed by visual analysis on scalp EEG by one board certified clinical neurophysiologist with independent confirmation of spikes by another board certified clinical neurophysiologist. The neurophysiologists were blinded to patient identifiers and surgical outcome. Selected EEG review included available random data from both wakefulness and sleep and was sampled throughout admission for a minimum of 1 h of EEG reviewed per patient. Selected random EEG was reviewed from both wakefulness and sleep and was sampled on days 1, 3, and 5 for a minimum of 20 min per day which equaled a minimum of 1 h of EEG reviewed per patient. EEG data obtained 1 h before or after a seizure was excluded to decrease the effect of seizures on spike frequency. Spikes were also noted as occurring in wakefulness or sleep, or both. Patients were classified into those with frequent spikes and those with infrequent spikes. In Krendl et al. [7], $\geq$60 spikes per hour was chosen as a specified cut off and thus a similar analysis was performed in this study. 12 random EEG samples were analyzed, with approximately half occurring during wakefulness and half during sleep for a total of 60 min per patient. Additionally, analysis of continuous data points was also performed to assess for trends in spike frequency and outcome. Postoperative seizure control was assessed at 1 year after resective epilepsy surgery using a modified Engel classification, as described previously. Non disabling auras without other seizures were considered seizure free. Class 1 patients were seizure free with or without auras, Class 2 patients experienced seizures less than 3 days a year or experienced purely nocturnal seizures, Class 3 patients showed a more than 80% decrease in seizure frequency, and Class 4 patients showed a less than 80% reduction in frequency.

## 3. Data analysis

Logistic regression analysis was used to assess the prognostic importance of clinical variables such as the presence or absence of MTS or GTC and pre-operative seizure frequency. An odds ratio was used to calculate seizure freedom at 1 year after surgery. Error probabilities $p < 0.05$ were considered significant. Pearson correlation and t-tests were used for analysis of continuous data, including spike frequency with clinical outcome and clinical variables.

## 4. Results

The initial query identified 56 patients who met these criteria. Four were excluded due to inadequate follow up and five due to insufficient monitoring data. Thus 47 patients (18 men, 29 women) were included in the study (see Table 1 for details). MRI brain

**Table 1**
Clinical characteristics of seizure free and non seizure free patients.

| | Sz free pts 1 yr after surgery N = 27 | Non-sz free pts 1 year after surgery N = 20 | Significance level |
|---|---|---|---|
| Age (year) | 20 | 16 | NS |
| Epilepsy duration (year) | 22 | 20 | NS |
| Women | 15 | 14 | NS |
| Men | 12 | 6 | NS |
| Abnormal unilateral PET (ispilateral hypometabolism) | 24 | 18 | NS |
| Abnormal unilateral MRI (ipsilateral MTS) | 15 | 14 | NS |
| Standard unilateral resection | 27 | 19 | NS |
| Preoperative seizure frequency >20 CPS/m | 0 | 4 | NS |
| GTC within 1 year prior to surgery | 5 | 9 | P = 0.061 |
| Total spikes/h (avg, range) | 56.9 (0–214) | 57.1* (0–5473) | NS |
| Awake spikes/h (avg, range) | 41.6 (0–269) | 42.2* (0–5299.5) | NS |
| Sleep spikes/h (avg, range) | 67.0 (0–155) | 76.5* (0–5820) | NS |

* Average values calculated excluding outlier (patient with 5473 total spikes).