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Seizure Outcome after Surgical Treatment for Temporal Lobe Epilepsy with Hippocampal Sclerosis

Tanatkan Kumpanont, M.D.
Teeradej Srikijvilaikul, M.D.
Department of Neurosurgery, Neurological Institute of Thailand, Bangkok, Thailand

Abstract

Objective: To study seizure outcomes in patients with temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS) and predictive factors associated with seizure outcome.

Material and Methods: One hundred and forty-seven patients with drug-resistance temporal lobe epilepsy with hippocampal sclerosis were retrospectively reviewed at Neurological Institute of Thailand between 2011 and 2021. All patients underwent temporal lobectomy and had pathologically proven hippocampal sclerosis. A minimum follow-up period was two years and seizure outcomes were classified as being seizure free and not seizure free using Engel's classification.

Results: A total of 109 patients were included in the study, there were 47 males and 62 females. The median follow-up duration was 4 years. Long-term seizure freedom at 2 years was 86.2% and at 5 years was 85.1%. Overall, 93 (85.3%) patients were seizure free (Engel I) at their last follow-up. Ninety-four (86.2%) patients were seizure free at a minimum of two years after surgery. Thirty-four patients were able to discontinue anti-seizure medication. There was 14% morbidity rate with no mortality. No predictive factors were found associated with seizure outcome in this study.

Conclusion: Temporal lobectomy is effective in drug-resistant temporal lobe epilepsy with hippocampal sclerosis. Favorable seizure free outcomes at least two years can be achieved. However, there are no predictive factors associated with seizure outcome in this study.

Keywords: Hippocampal sclerosis, Temporal lobe epilepsy, Drug-resistant epilepsy

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*Corresponding author: Tanatkan Kumpanont, M.D.

Introduction

Epilepsy is a chronic and debilitating condition that affects millions of people worldwide[1,2]. Temporal lobe epilepsy (TLE) is the most common type of epilepsy. Temporal lobe epilepsy with hippocampal sclerosis is the most common pathology frequently operated[3]. Patients with TLE-HS usually develop drug resistance[4,5]. With medical treatment alone, the remission rate for TLE-HS ranges from only 11 - 42%[6].

Surgery is now widely recognized as an effective and safe treatment option for patients whose seizures are not adequately controlled by medication[7]. Short-term outcomes following epilepsy surgery for TLE-HS are promising, with seizure freedom rates ranging from 70% to 90%[8,9]. Five-year follow-up studies report seizure freedom rates of 50% to 75%[10-12]. However, Seizure freedom when follow-up in longer term begins to decline[6].

This study aimed to evaluate seizure-free outcomes after a minimum of two years follow-up and to identify predictive factors associated with long-term seizures outcome.

Material and Methods

Patient and data

This study retrospectively reviewed patients with drug-resistant temporal lobe epilepsy associated with hippocampal sclerosis who underwent surgical treatment at Neurological Institute of Thailand during 2011 - 2021.

All patients underwent comprehensive presurgical evaluation including detailed history and examination, neuropsychological testing, 1.5 or 3.0 tesla magnetic resonance imaging (MRI) and 24-hour video-electroencephalography (EEG) monitoring. All patient's information were discussed at epilepsy management conference before surgery. If there was an undetermined or discordance imaging and video- EEG then an invasive EEG monitoring using either subdural electrodes, strip electrodes or depth electrodes were undertaken.

The inclusion criteria were as follows; (1) confirmed unilateral hippocampal sclerosis on MRI (2) pathologically confirmed hippocampal sclerosis (3) having completed minimum follow up period of two years. Patients with bilateral HS, Dual lesions on MRI, presence of other lesion on pathological examination or underwent selective amygdalohippocampectomy were excluded. All patients underwent standard anterior temporal lobectomy by a single neurosurgeon.

The data was gathered through comprehensive review of medical records, including clinical history, pre-operative evaluations, and postoperative clinical follow-up. Data collected including gender, age, age at seizure onset, age at surgery, side of surgery, duration of epilepsy, history of febrile seizure, family history of epilepsy, history of trauma, meningitis or encephalitis, history of secondary generalized tonic-clonic seizure, invasive EEG, postoperative seizure outcome and complications.

Seizure outcome

Seizure outcomes were assessed initially after surgery and during outpatient visit until the most recent follow-up using Engel's classification[13]. Seizure outcomes were classified into 4 classes; Class I (Free of disabling seizures, seizure free), Class II (Rare disabling seizures, almost seizure free), Class III (Worthwhile improvement) and Class

IV (No worthwhile improvement). Patients were categorized into 2 groups: Engel I was classified as seizure-free and Engel II-IV were not seizure free.

Statistical analysis

In this analysis, continuous variables were presented as median and interquartile range (IQR). Categorical variables were described with percentages. Differences in baseline characteristics between seizure status were analyzed using the Mann-Whitney U test for continuous variables and the Chi-square or Fisher's exact test was used for categorical variables. A univariate cox regression was used to examine the individual relationship between each variable and seizure-free status, those that achieved a *p*-value < 0.20 were selected for testing in multivariate cox regression. Hazard ratio (HR) and 95% confidence intervals (CIs) were used to illustrate the association between factors and seizure status. All probability values were two-sided and the significance level was set at p-value < 0.05. Statistical analyses were performed using SPSS for Windows version 16.0 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 147 patients with drug-resistance temporal lobe epilepsy associated with hippocampal sclerosis underwent temporal lobectomy between 2011-2021, 38 patients were excluded due to a loss of follow-up or lack of information in the medical record.

One hundred and nine patients (47 males and 62 females) met the inclusion criteria (Table1). The median age at seizure onset was 13 years (range 8 to 21.5 years). The median duration of epilepsy was 19 years (range 9 to 31 years). Median age at surgery was 35 years (range 26 to 47 years). The median duration of follow up was 4 years (range 2 to 6.5 years). Eighty-eight patients (90.7%) were right handedness.

Six patients had discordance data and underwent further invasive monitoring. Two patients had subdural electrode placement, 3 patients had bitemporal strip electrode placement and 1 patient had depth electrode placement. Fifty-eight patients (53.2%) were operated on the right.

Post-operative outcome

The seizure outcomes were classified by the Engel's classification as summarized in Table 2. Ninety-four patients (86.2%) were seizure free for at least two years. Ninety-three patients (85.3%) were seizure-free at their last follow up (Engel class I). The seizure free outcomes after surgery with yearly follow-up were as follows; 86.2% at 2 years, 92.5% at 3 years, 88.4% at 4 years, 85% at 5 years, 83.9% at 6 years, 82.5% at 7 years, 82.8% at 8 years, 76% at 9 years, 80% at 10 years, 87.5% at 11 years and 100% at 12 and 13 years (Table 3). The Kaplan-Meier curve shows overall survival of long-term seizure outcome (Figure 1). Seizure-free outcomes slightly decrease with longer follow-up period, 86.2% at 2 years, 85% at 5 years and 80% at 10 years. At last follow up, 34 patients were free from antiseizure medications.

Factors including age at epilepsy onset, duration of epilepsy, age at surgery, gender, side of surgery were not associated with seizure outcome. Additionally, other factors, including family history of epilepsy, history of trauma, history of febrile seizure, history of meningitis or encephalitis and his-

tory of secondary generalized tonic-clonic seizure were not predictive factors of seizure freedom.

There was no mortality in this study. Sixteen (14%) patients having post-operative complications including 9 patients with meningitis, 6 patients had hemorrhage either subdural or intracerebral hemorrhage and one with ischemic stroke. There was permanent neurological deficit in one patient.

Table 1 Characteristics of patients

Factors	Seizure free (n = 82)	Not seizure free (n = 27)	HR	95%CI	*p*-value
Sex (%)					0.331
Male	38 (46.3)	9 (33.3)	1.00	-	
Female	44 (53.7)	18 (66.7)	1.49	0.67 - 3.32	
Age at seizure onset (years; median, IQR)	12.0, (7.8-20.2)	15.0, (10.0-23.0)	1.01	0.98 - 1.04	0.69
Duration of epilepsy (years; median, IQR)	19.0, (10.0-30.0)	20.0, (6.0-32.0)	1.00	0.97 - 1.02	0.740
Age at surgery (years; median, IQR)	35.5, (26.0-48.2)	35.0, (26.0-46.0)	1.00	0.97 - 1.03	0.990
Side of operation (%)					0.556
Left	37 (45.1)	14 (51.9)	1.26	0.59 - 2.67	
Right	45 (54.9)	13 (48.1)	1.00	-	
History of febrile seizure	33 (40.2)	10 (37.0)	0.88	0.40 - 1.94	0.758
Family history of epilepsy	3 (3.7)	3 (3.7)	0.86	0.12 - 6.38	0.887
History of trauma	6 (7.3)	3 (11.1)	1.30	0.39 - 4.36	0.665
History of meningitis/encephalitis	6 (7.3)	3 (11.1)	1.54	0.46 - 5.11	0.484
History of 2nd generalized tonic-clonic seizure	32 (39.0)	16 (59.3)	1.86	0.86 - 4.00	0.115
Invasive monitoring	4 (4.9)	2 (7.4)	1.33	0.32 - 5.63	0.696

* Significant at 95% confidence interval ($p < 0.050$)

Table 2 Seizure outcome at last follow-up

Engel class	Patients (%)
I	93 (85.3)
II	6 (5.5)
III	9 (8.3)
IV	1 (0.9)
Total	**109**

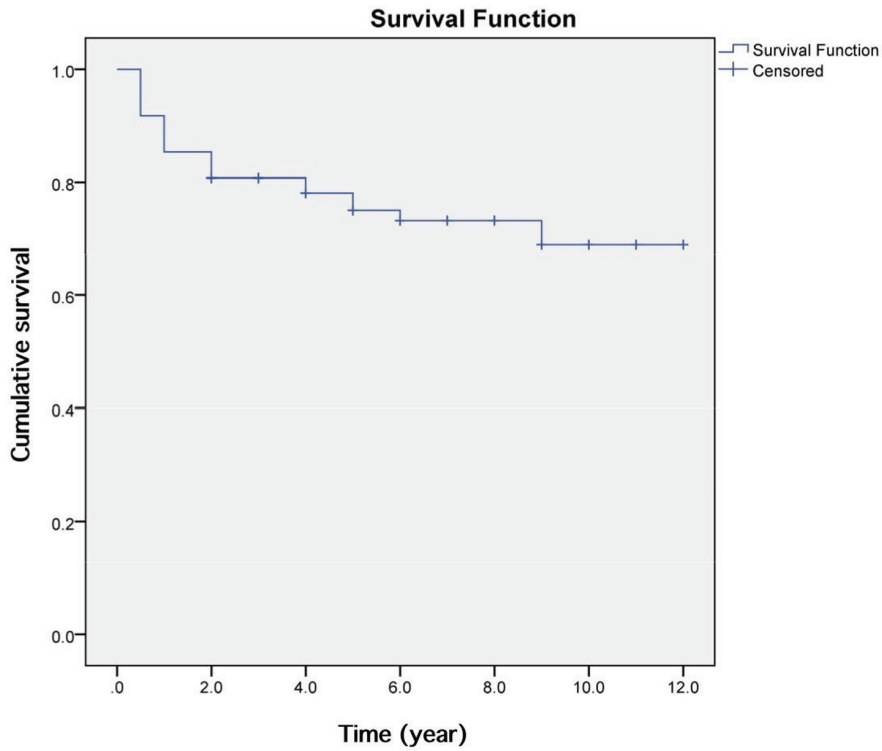

Figure 1 Kaplan-Meier curve of long-term seizure outcome

Table 3 The number of patients and seizure outcomes in longitudinal follow-up

Post-op year	Seizure free (%)	Not seizure free (%)	Total
2	94 (86.2)	15 (13.7)	109
3	87 (92.5)	7 (7.4)	94
4	69 (88.4)	9 (11.5)	78
5	57 (85)	10 (14.9)	67
6	47 (83.9)	9 (16)	56
7	33 (82.5)	7 (17.5)	40
8	29 (82.8)	6 (17.1)	35
9	19 (76)	6 (24)	25
10	12 (80)	3 (20)	15
11	7 (87.5)	1 (12.5)	8
12	4 (100)		4
13	1 (100)		1

Discussion

Overall seizure outcome

This study aims to assess long-term seizure outcomes in 109 patients who underwent temporal lobectomy with pathologically confirmed HS and had a minimum follow-up period of two years. Overall, 85.3% of patients had seizure freedom (Engel class I) at their last follow-up. Seizure freedom at 2 years and 5 years after surgery were 86.2% and 85.1% respectively. In our study, seizure outcomes were comparable to previous study which reported seizure freedom of 86% and 83% at 2 and 5 years[14,15]. This study also shows high rates of seizure freedom on a yearly basis which concur with previous report conducted in Thailand[16]. The Kaplan-Meier curve shows similar seizure-free outcomes at two and five years, followed by a slight decrease in seizure-free outcomes after five years, which then tends to stabilize over the long term. (Figure 1). This indicates that stable and favorable outcomes might be expected for patients who remain seizure-free five years after surgery. Small number of patients follow-up in longer term in our study might influence seizure outcomes. However, the seizure free outcomes in our study correlate with those of other studies[14,17] and confirm benefits of surgical treatment in drug-resistant temporal lobe epilepsy with hippocampal sclerosis.

Predictive factors for seizure outcome

Whether febrile seizure had an impact on seizure outcome of temporal lobe epilepsy with hippocampal sclerosis was still on debate. Dalio et al.[17] found that patients who reported a history of febrile seizure were likely to remain seizure free. One meta-analysis study (18) also concluded that febrile seizure correlates with good post-surgical outcome. Our study found no association between febrile seizures and seizure outcomes comparable to other study[19]. Since records from early childhood care of a number of patients were not available, data regarding the presence of febrile seizure as initial precipitating injuries might not be reliable enough.

History of secondarily generalized tonic-clonic seizures (2nd GTC) has been previously identified as a predictor of seizure recurrence after epilepsy surgery. Janszky et al.[20] reported that 2nd GTC seizures were associated with worse outcome at 2-year but not at 5-year following surgery for TLE-HS, possibly indicating more widespread cortical involvement and a distributed epileptogenic zone. However, other study[21] has reported the presence of 2nd GTC did not have any impact on seizure outcome similar with our findings in this study.

It has been hypothesized that early-onset seizures, characteristic of mesial temporal lobe epilepsy, were associated with better postoperative outcomes[22,23]. In this study, the median age of seizure onset was 12 years in seizure-free patients and 15 years in those who were not seizure-free. Although there was a trend suggesting that seizure-free patients had an earlier onset of seizures, the difference between the two groups was not statistically significant in our study.

Studies have suggested that a longer duration of epilepsy is associated with poor surgical outcomes[20], potentially due to the development of secondary epileptogenesis at sites distant from the primary lesion. However, our study found that epilepsy duration was not a predictive factor for seizure outcomes. This finding agrees with other

reports which found no association in epilepsy duration with seizure-free patients and those who continued to experience seizures[21].

Age at the time of surgery can influence different seizure outcomes. In our study, the median age at surgery was 35.5 years. This finding agrees with Sperling et al.[24] which reported seizure-free patients tended to be younger at the time of surgery.

Even though, many predictive factors were reported relating to surgical outcome in temporal lobe epilepsy with hippocampal sclerosis. We found no predictive factors associated with seizure outcome in this study similar to previous study by Aull-Watschinger et al.[25] and a study conducted in Thailand[26].

There were several limitations in this study included retrospective single cohort study and decreasing number of patients during longer follow-up period.

Conclusion

Seizure outcomes after surgery for temporal lobe epilepsy with hippocampal sclerosis had favorable outcome. Our findings including age at surgery, age of seizure onset, duration of epilepsy, presence of febrile seizures, and preoperative 2nd GTC seizures—were not predictive of seizure outcomes.

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