Outcomes after Temporal Lobectomy for Temporal Lobe Epilepsy with Hippocampal Sclerosis

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Objective: *Outcome predictors from the pure cohorts of patients with temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS) are limited. The aim of the present study was to assess seizure outcomes and predictive factors in groups of well-defined patients with TLE-HS.*
Material and Method: *One hundred forty eight patients with drug resistant TLE who had magnetic resonance imaging (MRI) that demonstrated unilateral HS underwent temporal lobectomy between 2004 and 2008 by a single neurosurgeon. All patients had completed at least two years of follow-up. Seizure outcome was categorized into seizure-free and not seizure-free.*
Results: *Ninety-five patients (64.2%) were seizure-free after surgery at two years of follow-up. At four years follow-up, 47 patients (77.1%) were seizure-free for at least two years. There was no operative mortality or significant morbidity. No clinical variables are predictive of surgical outcomes at two and four years of follow-up.*
Conclusion: *Temporal lobectomy for drug-resistant TLE with HS is safe and effective. The authors did not identify predictive factors of surgical outcomes in TLE-HS.*

Keywords: *Hippocampal sclerosis, Temporal lobe epilepsy, Drug resistant epilepsy surgery, Temporal lobectomy, Outcome, Predictors*

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Surgical treatment of epilepsy in Thailand has been performed for decades[1] but there were few reports of surgical outcome in Thai epileptic patients[2-4]. Surgical treatment of temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS) is the most common operation in drug-resistant epileptic patients. Predictors for the outcome after surgical operation from many studies vary from one to another; moreover, many studies included TLE patients with different etiologies[2]. There have been few studies on prognostic factors in TLE patients with HS (TLE-HS)[5-8].

TLE-HS is not a homogeneous syndrome. Preoperative investigations and selection of patients for surgery varies in many epilepsy centers. Identifying predictive factors for surgical outcome will help in counseling the patient before surgery. In the present study, the authors aimed to assess the longitudinal outcomes in patients with TLE-HS and identify predictors for seizure outcome after surgery in these groups of patients.

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Material and Method

The authors retrospectively studied patients with drug resistant TLE-HS who underwent anterior temporal lobectomy between 2004 and 2008 at King Chulalongkorn Memorial Hospital. Drug resistant epilepsy patients were defined as failure of adequate trials of two tolerated and appropriately chosen and used antiepileptic medications to achieve sustained seizure freedom[9]. All patients underwent pre-surgical evaluation including detailed history and physical examination, high-resolution magnetic resonance imaging (MRI), and prolonged video-EEG monitoring. Hippocampal sclerosis was defined when there was hippocampal atrophy on T1-weighted image, increased signal intensity on T2-weighted and FLAIR images. Positron emission tomography (PET), single photon emission computerized tomography (SPECT), and intracarotid sodium amytal testing were performed.

Patients were recruited under the following criteria: (1) aged > 16 years; (2) unilateral HS on MRI; (3) pathologically confirmed HS; (4) having completed at least two years of follow-up. Patients were excluded if they had bilateral HS, other MRI lesions, or having taken selective amygdalohippocampectomy.

Patients were considered surgical candidates if noninvasive data revealed concordance of EEG and MRI or concordance of invasive EEG and MRI and under the consensus at epilepsy patient management conference.

All patients underwent anterior temporal lobectomy (ATL) by the same neurosurgeon (TS). Anterior temporal lobectomy involved standard removal of temporal neocortex measuring 4 cm (dominant temporal lobe) and 5 cm (nondominant temporal lobe) from the anterior temporal fossa along the middle temporal gyrus. The hippocampus was removed as far back as the level of superior colliculus. The authors did not use intraoperative electrocorticography to tailor the resection.

Invasive EEG monitoring was undertaken when pre-surgical evaluation findings were conflicting or indeterminable. Seizure outcome was assessed at their visits to the outpatient clinic at two and four years after surgery and classified according to Engel's classification[10], which was categorized into seizure-free (Engel 1) and not seizure-free (Engel 2-4). The seizure-free outcome was defined when the patients had no seizures for at least two years.

The present study has been approved by the institutional review board (IRB) of the Faculty of Medicine, Chulalongkorn University.

The authors performed a univariate analysis to assess the prognostic significance of the clinical variables, and the authors calculated the odds ratios (OR) for a seizure-free outcome at two and four years after surgery. The significance level (p) was set at 0.05.

Results

One hundred forty eight patients (77 females, 71 males) with drug resistant TLE-HS, who also completed at least two years follow-up and met the inclusion criteria, were recruited. The mean age at the onset of epilepsy was 14.2 ± 9.3 years (range 1 month to 51 years), and the mean epilepsy duration was 20.7 ± 10.0 years (range 2-52 years). The mean age at surgery was 34.9 ± 9.7 years (range 17-62 years). The mean duration of follow-up was 3.6 ± 1.1 years (range 2-6 years).

Sixty-three patients were operated on the right side, 85 patients were operated on the left (Table 1). Ninety-one patients had preoperative concordance of interictal EEG (> 90% ipsilateral to HS), ictal EEG and MRI on the same side of temporal lobectomy. Invasive monitoring using bitemporal subdural strip electrodes was performed on seven patients. There was no operative mortality or significant neurological deficit detected. At the last follow-up, 33 patients (22.3%) were able to discontinue antiepileptic drugs (AEDs) for at least one more year.

Ninety-five patients (64.2%) were seizure-free after surgery at two years of follow-up (Engel Class 1, 64.2%; Class 2, 20.9%; Class 3, 12.2%; Class 4, 2.7%). At four years follow-up, 47 patients (77.1%) were seizure-free for at least two years (Engel Class 1,

Table 1. Demographic and clinical characteristics of patients with TLE-HS

	Number of patients (%)
Total	148
Sex (female/male)	77 (52.0%)/71 (48.0%)
Side of operation (right/left)	63 (42.6%)/85 (57.4%)
Mean age at epilepsy onset (years)	14.2 ± 9.3 (range 1 month-51 years)
Mean duration of epilepsy (years)	20.7 ± 10.0 (range 2-52 years)
Mean age at surgery (years)	34.9 ± 9.7 (range 17-62 years)
Mean follow-up (years)	3.6 ± 1.1 (range 2-6 years)
Febrile seizures	98 (66.2%)
Family history for epilepsy	30 (20.3%)
History of status epilepticus	11 (7.4%)
History of meningitis/encephalitis	10 (6.7%)
History of SGTCS	83 (56.1%)

SGTCS = secondarily generalized tonic-clonic seizures

77.1%; Class 2, 9.8%; Class 3, 11.5%; Class 4, 1.6%). Three seizure-free patients (5%) changed their outcomes at 4-year follow-up, and 13 patients (21.3%) who were not seizure- free became seizure- free at four years of follow-up.

The univariate analysis revealed that clinical variables such as age of onset, duration of epilepsy, age at surgery, gender, side of surgery, family history of epilepsy, history of febrile seizures, history of status epilepticus or meningitis/encephalitis, and history of secondarily generalized tonic-clonic seizures (SGTCS) were not predictive of seizure outcome (Table 2).

Discussion

The outcomes of seizure in the present study concur with recently reports on surgically treated hippocampal sclerosis patients when the outcomes of seizure were evaluated by longitudinal follow-up instead of cross-sectional method based on the last available follow-up[11-13]. Previous reports of temporal lobectomy in Thailand[2,3] included heterogenous pathologies and included few patients with cross-sectional follow-up. The percentages of seizure-free outcomes at year 2 are less than that at year 4 because a number of patients who had some early postoperative seizures became seizure-free at four years of follow-up. Some patients were seizure free after medication adjustment but in some patients running down phenomenon[14] may account for this. Few patients changed their outcome after a seizure-free period of two years.

Many predictive factors were reported related to surgical outcome in TLE, but there have been few reports on factors related to surgical outcomes in TLE-HS. Predictors of outcomes is in the literatures were inconclusive. Longer epilepsy duration, febrile seizures, and older age at surgery were associated with worse outcomes after surgery in TLE-HS[7,12]. Others found seizure frequency, the duration of epilepsy, and history of febrile seizures not associated with the outcomes in TLE-HS[5,15]. Hardy[5] reported history of status epilepticus was the only predictive factor of outcome after surgical treatment of TLE-HS. Tezer[11] found early seizure during the first month after surgery was predictive of worse outcome in TLE-HS. The presence of SGTCS suggests a more wide spread epileptogenic zone or secondarily epileptogenesis. Janszky[7] found the history of SGTCS was associated with worse outcome at 2-year outcome but not at 5-year postoperatively. In contrast, other reported the presence of SGTCS did not have an impact on outcome at any time point[12].

The present study shows that many clinical variables do not predict the outcome after temporal

Table 2. Univariate analysis of clinical variables at year 2 after surgery

	Seizure-free, n (%)	Not seizure-free, n (%)	p-value	OR (95% CI)
Gender			0.221	0.66 (0.33-1.29)
Females	53 (55.79)	24 (45.28)		
Males	42 (44.21)	29 (54.72)		
Febrile	67 (70.53)	31 (58.49)	0.139	1.70 (0.84-3.43)
Family history	18 (18.95)	12 (22.64)	0.592	0.80 (0.35-1.82)
Encephalitis	9 (9.47)	1 (1.89)	0.113	5.44 (0.67-44.19)
Status epilepticus	8 (8.42)	3 (5.66)	0.542	1.53 (0.39-6.04)
Side of Surgery			0.589	1.21 (0.61-2.39)
Left	53 (55.79)	32 (60.38)		
Right	42 (44.21)	21 (39.62)		
Invasive	3 (3.16)	4 (7.55)	0.242	0.40 (0.09-1.86)
SGTCS	50 (52.6)	33 (62.3)	0.259	0.673 (0.34-1.34)
	Mean (SD)	Mean (SD)		
Onset	14.21 (9.38)	14.09 (9.23)	0.943	1.00 (0.97-1.04)
Duration	20.09 (10.43)	21.89 (9.15)	0.296	0.98 (0.95-1.02)
Age of surgery	34.40 (9.83)	35.77 (9.41)	0.407	0.99 (0.95-1.02)
Length of follow-up	3.43 (1.10)	3.76 (1.19)	0.092	0.77 (0.57-1.04)

SGTC = secondarily generalized tonic-clonic seizures

lobectomy for HS, which in agreement with a previous report[13]. The present study did not investigate postoperative seizures as a predictor because the authors classified all patients who had early postoperative seizures in the not seizure-free group.

Pre-surgical identification of unilateral hippocampal atrophy, or of IEDs that are all concordant with ictal onset, predict excellent outcome in the series of temporal lobectomy[16]. A good surgical outcome was obtained when MRI and IEDs were used in combination, compared to other combinations of MRI and EEG results[17]. The authors did not study the predictive factor of interictal EEG or ictal EEG and outcome but 61% of patients had all concordant data preoperatively. The rest of the patients had either interictal EEG, ictal EEG concordant with MRI or non-localized data. The present study is a retrospective study, the authors could not investigate the predictive factor of electrophysiologic data because there were small numbers of patients in each subgroup for statistical analysis. Furthermore, there was selection bias in patient's selection in the group of discordance for surgery.

Previous reported in the literatures suggested that the presence of HS on MRI might be the most important positive prognostic factor after temporal lobectomy[16,18-22]. The present study did not identify any clinical variables predictive of surgical outcome. MRI demonstrated unilateral HS itself might be predictive of outcome in selected patients.

Conclusion

Temporal lobectomy for TLE-HS is safe and effective. No clinical factors are predictive of seizure outcome in patients with unilateral HS. In selected patients with a clinical history suggestive of TLE, the presence of unilateral HS on MRI may be a potent preoperative factor of surgical outcome.

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Potential conflicts of interest

None.

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ผลการผ่าตัดสมองด้านข้างในผู้ป่วยโรคลมชักจากแผลเป็นสมองด้านข้าง

ธีรเดช ศรีกิจวิไลกุล, สุกัลยา เลิศล้ำ, สุภัทรพร เทพมงคล, ชนพ ช่วงโชติ

วัตถุประสงค์: *การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาปัจจัยที่มีผลต่อการผ่าตัดผู้ป่วยโรคลมชักเฉพาะกลุ่มที่มีจุดกำเนิดการชักจากแผลเป็นสมองด้านข้าง ซึ่งมีการศึกษาในปัจจุบันไม่มากนัก*

วัสดุและวิธีการ: *การศึกษาย้อนหลังในผู้ป่วยโรคลมชักที่ภาพแม่เหล็กไฟฟ้าแสดงแผลเป็นในสมองด้านข้างเพียงข้างเดียว และได้รับการผ่าตัดสมองด้านข้างระหว่างปี พ.ศ. 2547-2551 จำนวน 148 ราย โดยประสาทศัลยแพทย์คนเดียว ผู้ป่วยทั้งหมดได้รับการติดตามผลการผ่าตัดอย่างน้อย 2 ปี และจัดแบ่งผลการผ่าตัดเป็นผู้ป่วยที่ไม่มีอาการชักและผู้ป่วยที่ยังมีอาการชักหลังผ่าตัด*

ผลการศึกษา: *ผู้ป่วย 95 ราย (64.2%) ไม่มีอาการชักหลังผ่าตัดเมื่อติดตามผลการรักษา 2 ปีแรก และผู้ป่วย 47 ราย (77.1%) ไม่มีอาการชักอย่างน้อย 2 ปี เมื่อติดตามผลการผ่าตัดเป็นระยะเวลา 4 ปีหลังผ่าตัด ไม่มีผู้ป่วยเสียชีวิตหลังผ่าตัดหรือพิการถาวร ไม่พบปัจจัยทางคลินิกที่มีผลต่อผลการผ่าตัด*

สรุป: *การผ่าตัดสมองด้านข้างในผู้ป่วยโรคลมชักจากแผลเป็นสมองด้านข้างมีความปลอดภัยและได้ผลการผ่าตัดดี ไม่พบปัจจัยทางคลินิกที่มีผลต่อการผ่าตัด*