Original Article

Long-Term Seizure Outcome after Temporal Lobectomy for Hippocampal Sclerosis

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Objective: To study long-term seizure outcomes in patients with temporal lobe epilepsy [TLE] with hippocampal sclerosis [HS].

Materials and Methods: One hundred twelve patients with drug resistant TLE underwent temporal lobectomy and had pathologically proven HS between 2004 and 2008. All patients had a minimum follow-up of five years. Seizure outcome was categorized into being seizure-free and not seizure-free.

Results: Sixty one patients (54.5%) were seizure free for the entire period after surgery. One hundred patients (89.3%) were seizure free for at least two years at the last follow-up. Forty three patients (38.4%) were able to stop antiepileptic medications. The mean follow-up was 8.1±1.9 years (range 5 to 11 years). A preoperative secondarily generalized tonic-clonic seizure was predictor for poor seizure outcome.

Conclusion: A long-term outcome (more than five years) in terms of a percentage of seizure free in TLE with HS [TLE-HS] patients remains favorable. Long-term seizure outcome is helpful for preoperative and postoperative counseling to the patients. Surgical treatment should be considered in patients with drug-resistant TLE-HS.

Keywords: Hippocampal sclerosis, Temporal lobe epilepsy, Temporal lobe surgery, Epilepsy surgery, Seizure outcomes

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Surgical treatment of temporal lobe epilepsy [TLE] is beneficial for patients with drug-resistant epilepsy. A randomized controlled trial reported that surgical treatment of TLE was superior to medical treatment[1]. Hippocampal sclerosis [HS] is the most common cause of drug-resistant TLE referring for surgery. Seizure outcome after temporal lobectomy for HS showed favorable outcome providing 60% to 80% seizure-free outcome[2-6].

Many studies reported seizure outcome at the time of last follow-up and included various etiologies of TLE. Few studies reported long-term seizure outcome more than five years after surgery for TLE-HS[5]. A number of patients with TLE-HS have recurrence of seizures after long-term follow-up and some with early postoperative seizures subsequently become seizure-free (running down phenomenon)[7,8]. Long-term seizure outcome after surgery is important in terms of preoperative and postoperative patient counseling. The aim of the present study is to: 1) report seizure outcome at extended period of follow-up from our previous cohort in TLE-HS patients after temporal lobectomy[6], and 2) attempt to identify the potential predictors of long-term seizure outcome.

Materials and Methods

The authors studied seizure outcomes in 112 patients operated for drug-resistant TLE-HS at King Chulalongkorn Memorial Hospital between 2004 and 2008. All patients had a minimum of 5-year follow-up. They comprised of 75.6% the original cohort reported previously[6]. All surgeries were performed by a single neurosurgeon (Srikijvilaikul T). They have been followed-up in two institutes, which were the Prasat Neurological Institute and King Chulalongkorn Memorial Hospital.

Preoperative evaluations included 24-hour video-electroencephalography [EEG] monitoring and 1.5 tesla magnetic resonance imaging [MRI]. Invasive EEG monitoring was performed in patients with discordant or inconclusive data. Details of the surgical

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techniques had been described in a previous study[6]. Inclusion criteria included patients older than 16 years, unilateral HS on MRI, pathologically confirmed HS, and having at least five years of follow-up. Patients were excluded if they had bilateral HS, other MRI lesions, or have been operated with selective amygdalo-hippocampectomy. Invasive EEG monitoring was performed in eight patients, six patients had bitemporal strip electrode placement and two patients had subdural electrode placement.

Data and seizure outcomes was collected prospectively since 2004 until the time of study analysis in two institutes as mentioned above. Outcome status was determined each year from five years up to eleven years after surgery. Seizure outcome was classified according to Engel's classification[9] and categorized into being seizure free (Engel I) and not seizure free (Engel II-IV).

The present study had been approved by the Institutional Review Board [IRB] of the Faculty of Medicine, Chulalongkorn University and Prasat Neurological Institute.

Statistical methods

Mann-Whitney U test and independent t-test were used for continuous variables. Chi-square or Fisher's exact test was used for categorical variables. Univariate logistic regression analysis was used to assess the prognostic significance of the clinical factors. The significance level (p) was set at 0.05.

Results

One hundred twelve patients (63 females, 49 males) met the inclusion criteria. The mean age at epilepsy onset was 14.7±9.8 years (range 1 month to 51 years). The mean duration of epilepsy was 20.7±9.8 years (range 3 to 48 years). Mean age at surgery was 35.2±9.8 years (range 17 to 62 years). The mean duration follow-up was 8.1±1.9 years (range 5 to 11 years) (Table 1). There were no demographic or clinical factors difference between the present cohort and the patients who had follow-up less than five years.

At the last follow-up, 100 patients (89.3%) were seizure free for at least two years. The postsurgical seizure-free outcomes yearly were as follows, 83% at 5 years, 82.1% at 6 years, 80.5% at 7 years, 76% at 8 years, 77.4% at 9 years, 74.4% at 10 years, and 100% at 11 years after surgery (Table 2).

When we assessed seizure-free outcome throughout the available follow-up period, sixty one patients (54.5%) were seizure free since surgery (Table 3). Seizure free outcome since surgery were as follows, 51.8% at 5 years, 52.6% at 6 years, 48.3% at 7 years, 49.3% at 8 years, 49.1% at 9 years, and 53.5% at 10 years after surgery. Changes of seizure outcome during follow-up period could be observed in this cohort.

Thirty-six patients were excluded from the study because having follow-up time less than five years. In these patients, 31 patients (86.6%) were seizure free since surgery, nine patients had four years seizure-free, 16 patients had three years seizure-free, and six patients had two years seizure-free. Eighteen patients (16.1%) had seizures in the first two years after surgery and became seizure free since then until the last follow-up.

When analyzing outcome at the last follow-up, 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

Table 1. Demographic and baseline characteristics of 112 patients with TLE-HS

	n = 112
Sex, n (%)	
Female	63 (56.2)
Male	49 (43.8)
Age at seizure onset, mean ± SD	14.7±9.8
Duration of epilepsy, mean ± SD	20.7±9.8
Age at surgery, mean ± SD	35.2±9.8
Follow-up time, mean ± SD	8.1±1.9
Side of operation, n (%)	
Right	46 (41.1)
Left	66 (58.9)
Febrile seizure, n (%)	73 (65.2)
Family history of epilepsy, n (%)	24 (21.4)
History of status epilepticus, n (%)	11 (9.8)
History of meningitis/encephalitis, n (%)	5 (4.5)
History of SGTCS, n (%)	62 (55.4)

TLE-HS = temporal lobe epilepsy with hippocampal sclerosis; SGTCS = secondary generalized tonic-clonic seizures

Table 2. The number of patients and seizure outcomes in longitudinal follow-up

Years of follow-up	Seizure free n (%)	Not seizure free n (%)	Total
5	93 (83.0)	19 (17.0)	112
6	78 (82.1)	17 (17.9)	95
7	70 (80.5)	17 (19.5)	87
8	57 (76.0)	18 (24.0)	75
9	41 (77.4)	12 (22.6)	53
10	32 (74.4)	11 (25.6)	43
11	3 (100)	-	3

of status epilepticus, or meningitis/encephalitis, and history of secondary generalized tonic-clonic seizures [SGTCS] was not predictive of seizure outcome. When analyzing seizure outcome since surgery, history of SGTCS was associated with poor seizure free outcome ($p = 0.028$) (Table 3).

Discussion

Eighty-nine percent of patients were seizure free for at least five years. Long-term seizure-free outcomes at 5-years and 10-years after surgery were 83% and 74.4%, respectively. The long-term seizure free outcome in the present study agrees with other studies[2,4,9]. Long-term seizure-free outcome declines slightly, and changes of seizure outcome can be observed during follow-up similar to the authors' study[10].

When using seizure-free outcome throughout the available follow-up period, 54.5% of patients were seizure free since surgery, which is similar to other studies[2,5,11]. The percentage of seizure-free patients was comparable to the randomized controlled trial of temporal lobe surgery and still better than medical treatment[1]. Sixteen percent of the patients had seizures in the first two years after surgery and exhibited running down phenomenon[8], where later they gradually became seizure free. Antiepileptic drugs [AEDs] were able to be discontinued in 30 patients (26.7%). A few patients preferred continuing low dose of AED instead of discontinuing the medications.

The surgical outcomes may differ when using different classification[2]. Aull-Watschinger et al[3] reported similar results to the authors' study when they used more stringent classification[12]. In their study, the percentage of seizure-free patients was 70% to 79% when included the patients with auras in a seizure-free group, but decreased from 64.4% at year one to 45.8% at year five with more stringent classification when absence of both seizures and auras after operation is required for a seizure freedom.

Previous studies regarding outcome and predictive factors for outcome after temporal lobectomy were often contradictory[14,15]. The timing of outcome assessment on postoperative course has effect on seizure outcome and predictive factors. Many temporal lobe surgery studies included various pathologies, short-term follow-up, and cross-sectional follow-up. The authors reported longitudinal outcomes and in homogeneous group of TLE-HS operated by the same neurosurgeon.

The authors did not find clinical variables predictive of outcome in previous study[6]. The authors did not find clinical factors associated with outcomes when analyzed at the time of the last available follow-up in the present study. SGTCS was the only poor prognostic

Table 3. Demographic and analysis of outcomes and variables for patients who had seizure-free throughout surgery and had a minimum follow-up of 5 years

	Outcome		p-value	OR	95% CI
	All Seizure free (n = 61)	Not all seizure free (n = 51)			
Sex, n (%)			0.073	1.994	0.934 to 4.258
Female	39 (63.9)	24 (47.1)			
Male	22 (36.1)	27 (52.9)			
Age at onset			0.710	1.004	0.966 to 1.043
Median (interquartile range)	12.0 (7.5 to 19.5)	14.0 (9.0 to 19.0)			
Mean ± SD	14.5±9.9	14.9±9.7			
Duration of epilepsy, mean ± SD	19.4±9.3	22.2±10.2	0.141	1.030	0.990 to 1.071
Age at surgery, mean ± SD	33.9±10.5	36.8±8.9	0.121	1.031	0.992 to 1.072
Side of surgery, n (%)			0.715	0.868	0.407 to 1.852
Left	35 (57.4)	31 (60.8)			
Right	26 (42.6)	20 (39.2)			
Febrile seizure, n (%)	43 (70.5)	30 (58.8)	0.197	0.598	0.273 to 1.309
Family history of epilepsy, n (%)	13 (21.3)	11 (21.6)	0.974	1.015	0.410 to 2.512
History of status epilepticus, n (%)	7 (11.5)	4 (7.8)	0.520	0.657	0.181 to 2.383
History of encephalitis, n (%)	4 (6.6)	1 (2.0)	0.374	0.285	0.031 to 2.635
History of SGTCS, n (%)	28 (45.9)	34 (66.7)	0.028*	2.357	1.092 to 5.090
History of head injury, n (%)	13 (21.3)	7 (13.7)	0.332	0.587	0.215 to 1.606

SGTCS = secondary generalized tonic-clonic seizures

* Statistically significant

factor when seizure free throughout the follow-up period was assessed. McIntosh et al[13] in the series of inhomogeneous pathologies reported that the presence of preoperative SGTCS was associated with seizure recurrence after temporal lobectomy. Predictors for long-term outcome of TLE-HS are different from those variables that predict the short-term outcome[3,14].

Janszky et al[16] reported the presence of SGTCS and ictal dystonia predicted the 2-year outcome, but longer epilepsy duration predicted a poor 5-year outcome. Pre-surgical SGTCS and aura were significantly associated with unfavorable outcome in International League Against Epilepsy [ILAE] classification at the end of first and last follow-up[2]. In the longitudinal outcome up to 18 years with exclusively TLE-HS patients, the presence of SGTCS tended to have seizure recurrence[5]. Jeong et al[9] reported younger age at surgery, absence of SGTCS, and HS on MRI were significant predictors of good surgical outcome. SGTCS may indicate a more widespread epileptogenic zone or of secondary epileptogenesis. SGTCS may be a poor prognostic factor after long-term follow-up after temporal lobectomy for TLE-HS.

The current study has some limitations. First, the study was a retrospective study and 36 patients were excluded from the cohort because their follow-up periods were less than five years. In these group of patients, 86.6% were seizure free since surgery and may affect seizure outcome and predictive factors. It was possible that they were seizure-free and did not want to come to the hospital. Secondly, the impact of postoperative AED treatment on postoperative outcome could not be assessed. AED treatment may affect the outcome in some patients with early postoperative seizures not the running down phenomenon alone. Thirdly, preoperative MRI at the timing of surgery was 1.5 Tesla MRI, which might not exclude the case with bilateral HS or other subtle lesions.

Conclusion

Long-term seizure outcome after temporal lobectomy for TLE-HS remains favorable. Outcome classification and the timing of outcome assessment may affect the seizure-free rate and prognostic factors. Temporal lobectomy should be considered in the patients with drug-resistant TLE-HS.

What is already known on this topic?

Seizure outcome after temporal lobectomy for HS is good. The percentage of seizure-free declines when follow-up for more than five years but remains favorable. There were few reports of outcome after surgery in a homogeneous group of TLE from HS and longitudinal follow-up.

What this study adds?

This study reports long-term seizure outcome in the cohort of TLE-HS patients previously reported[6]. This is the first report of long-term outcome after temporal lobectomy for TLE-HS in Thailand, and the results were comparable to the other publications. The results will be beneficial for counseling or referring the patients who were refractory to medical treatments to surgical treatment.

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Potential conflicts of interest

None.

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ผลการผ่าตัดสมองด้านข้างระยะยาวในผู้ป่วยโรคลมชักจากแผลเป็นสมองกลีบข้าง

ธีรเดช ศรีกิจวิไลกุล, ชูศักดิ์ ลิโมทัย

วัตถุประสงค์: เพื่อศึกษาผลระยะยาวของการผ่าตัดสมองกลีบข้างในผู้ป่วยโรคลมชักที่มีจุดกำเนิดการชักที่ฮิปโปแคมปัส

วัสดุและวิธีการ: ศึกษาในผู้ป่วยโรคลมชักจากแผลเป็นสมองกลีบข้างที่ได้รับการผ่าตัดระหว่าง พ.ศ. 2547 ถึง พ.ศ. 2551 และได้ติดตามผลการรักษาไม่น้อยกว่า 5 ปี จำนวน 112 ราย ผลการผ่าตัดแบ่งเป็นกลุ่มที่ไม่มีอาการชัก และกลุ่มที่ยังมีอาการชักหลังผ่าตัด

ผลการศึกษา: ผู้ป่วย 61 ราย (54.5%) ไม่มีอาการชักอีกเลยหลังการผ่าตัด และในการติดตามผู้ป่วยครั้งสุดท้าย มีผู้ป่วย 100 ราย (89.3%) ไม่มีอาการชักอย่างน้อย 2 ปี มีผู้ป่วย 43 ราย (38.4%) สามารถหยุดยากันชักได้ ค่าเฉลี่ยระยะเวลาในการติดตามผู้ป่วย 8.1±1.9 ปี ผู้ป่วยที่มีประวัติเกร็งกระตุกแบบทุติยภูมิเป็นปัจจัยที่ทำให้มีการพยากรณ์โรคไม่ดี

สรุป: การผ่าตัดผู้ป่วยโรคลมชักจากแผลเป็นสมองกลีบข้างในระยะยาว (มากกว่า 5 ปี) ได้ผลดี การให้คำปรึกษาผู้ป่วยโรคลมชักจากแผลเป็นสมองกลีบข้างทั้งก่อนผ่าตัดและหลังผ่าตัด มีประโยชน์อย่างยิ่ง และการผ่าตัดสมองกลีบข้างควรเป็นทางเลือกในการรักษาผู้ป่วยที่ไม่ตอบสนองต่อยากันชัก