Turk Neurosurg 33(1):101-109, 2023

Original Investigation

DOI: 10.5137/1019-5149.JTN.34458-21.2

Received: 06.03.2021
Accepted: 06.05.2022

Published Online: 30.11.2022

Surgical Outcome of Young and Adult Patients with Temporal Lobe Epilepsy Related to Hippocampal Sclerosis in Modern Era

Semih Can CETINTAS[1], Tufan Agah KARTUM[1], Taha Sukru KORKMAZ[1], Rahsan KEMERDERE[1], Seher Naz YENI[2], Taner TANRIVERDI[1]

[1]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Neurosurgery, Istanbul, Turkey
[2]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Neurology, Istanbul, Turkey

Corresponding author: Semih Can CETINTAS ✉ semihcan1992@gmail.com

ABSTRACT

AIM: To evaluate the preoperative, operative, and postoperative outcomes of young and adult patients who underwent surgery for temporal lobe epilepsy related to hippocampal sclerosis (TLE-HS).

MATERIAL and METHODS: This retrospective study assessed prospectively registered data collected from 2010 to 2020. Clinical, electrophysiological, pathological, and postoperative outcomes were evaluated and compared. Post-surgical seizure outcome was classified into continuous seizure freeness without aura and relapse.

RESULTS: In total, 16 young and 48 adult patients with TLE-HS were included in the analysis. The clinical, electrophysiological, pathological, and postoperative outcomes were similar between the young and adult groups. However, the seizure outcome did not significantly differ between the two groups (p=0.38). A significant proportion of patients in both groups were satisfied with the surgical outcomes.

CONCLUSION: Surgery is extremely effective against TLE-HS in young patients, as in adults. Furthermore, the clinical, radiological, and pathological outcomes are similar between young and adult patients with TLE-HS.

KEYWORDS: Adult patients, Seizure outcome, Surgery, Temporal lobe epilepsy, Young patients

ABBREVIATIONS: AED: Antiepileptic drug, **ATL:** Anterior temporal lobectomy, **CP:** Complex partial, **CAH:** Cortico-amygdalohippocampectomy, **DE:** Depth electrode, **EEG:** Electroencephalography, **FC:** Febrile convulsion, **FCD:** Focal cortical dysplasia, **GTC:** Generalized tonic-clonic, **HS:** Hippocampal sclerosis, **MRI:** Magnetic resonance imaging, **mMCD:** Mild malformation of cortical development, **PET:** Positron emission tomography, **QoL:** Quality of life, **TLE:** Temporal lobe epilepsy

INTRODUCTION

Epilepsy is one of the most common neurological disorders and has a severely negative impact on the quality of life (QoL) of patients and their families. Approximately two-thirds of patients with epilepsy present with focal epilepsy, and temporal lobe epilepsy (TLE) is the most common type. Over the years, tissue samples collected during surgeries conducted at major epilepsy centers worldwide were assessed. Results showed that hippocampal sclerosis (HS) is the most common pathological substrate. Accordingly, TLE related to HS (TLE-HS) is a progressive degenerative disease. Thus, the term temporal lobe sclerosis has been introduced in the epilepsy literature (20). Prospective, randomized, con-

Semih Can CETINTAS : 0000-0001-6036-164X
Tufan Agah KARTUM : 0000-0003-1529-6476
Taha Sukru KORKMAZ : 0000-0002-5678-257X
Rahsan KEMERDERE : 0000-0002-9947-3486
Seher Naz YENI : 0000-0001-7372-5430
Taner TANRIVERDI : 0000-0002-1878-0696

trolled clinical trials have shown that surgery is associated with a significantly better seizure outcome compared with antiepileptic drug (AED) treatment in patients with TLE. Similar to adult or older patients, children have favorable seizure and cognitive outcomes postoperatively. Thus, surgery is widely performed for early-stage TLE (5,19,21). Furthermore, it can improve the QoL of patients who were seizure-free at the long-term follow-up (19).

In the current literature, surgical outcome including QoL has been assessed extensively and compared between children or adolescents and adult or older patients with TLE. Results showed that surgery has a positive impact on the outcomes of each age group (3,5,8,13). Notably, HS is not a common pathological substrate after TLE surgery in children with focal cortical dysplasia (FCD) or neuroepithelial tumors such as dysembryoplastic lesions and gangliogliomas. Furthermore, the interpretation of seizure semiology, radiological and electrophysiological findings, cognition, and QoL between children and adults may be challenging because of differences in etiology, pathology, and life expectancy. Moreover, the proportion of adult patients who are seizure-free at the long-term follow-up after TLE surgery has been declining annually. However, the rates remained constant in children (16,18).

In recent years, the surgical outcomes of children and adults with TLE have been compared. However, the number of studies is limited. Almost all reports comparing the surgical outcome of TLE between children and adults included multiple etiologies such as FCD, seizure-related tumors, and vascular lesions (3,5,8,13). In addition, there has been no report comparing the long-term surgical outcome of TLE-HS in young and adult patients. Therefore, to address this gap, the current retrospective study aimed to assess patients with TLE-HS using prospectively registered data.

MATERIAL and METHODS

This study was approved by the Local Ethics Committee of Cerrahpasa Medical Faculty, Istanbul University-Cerrahpasa, Istanbul, Turkey and did not contain any data exposing patient identity (Date: 20.01.2021; No: 11876). All patients provided a written informed consent prior to surgery.

Patients

Patients who underwent TLE-HS surgery between February 2010 and July 2020 at our epilepsy center, which is one of the few prominent tertiary centers in Turkey, were included in the analysis. The seizure and clinical outcomes of young and adult patients were compared. The participants were then classified into the young (17–24 years) and adult (25–56 years) groups. In particular, patient classification according to age did not meet the criteria of the formal nomenclature of the World Health Organization or the United Nations because the number of participants was limited and, more importantly, consecutive patients underwent surgery at the age of 17–56 years. The following inclusion criteria were applied stringently: patients without temporal pathologies on preoperative magnetic resonance imaging (MRI) such as heterotopia, cavernoma, and tumor; those who underwent anterior temporal lobectomy (ATL) alone; those with histologically diagnosed TLE-HS; and those with complete follow-up data. Meanwhile, patients who had tumor or vascular lesions on either the temporal neocortex or the mesial structures were excluded.

Methods

All patients at tertiary epilepsy centers undergo a detailed diagnostic work-up, and the decision to perform surgery is discussed during local epilepsy meetings held once a week. Data about the medical history of patients, seizure semiology, and results of electrophysiological studies including scalp electroencephalography (EEG) and/or invasive EEG (such as depth electrode [DE] insertion, as indicated) and radiologic and/or functional studies including 1.5T or 3.0T (since 2018) head MRI with epilepsy protocol and positron emission tomography (PET) were obtained. Some patients required functional MRI to lateralize speech and memory functions. At our center, DE insertion is not performed routinely on each patient with TLE-HS unless there are concordant data between seizure semiology and radiological and electrophysiological results. In particular, patients with bilateral TLE-HS underwent PET and/or DE to lateralize and/or localize the epileptogenic temporal side. Each patient was closely followed-up by our expert neurologists/epileptologists who manage their treatment and evaluate seizure outcome postoperatively. Follow-ups were performed every 3 months within the first year postoperatively and annually thereafter.

The following data were obtained: age at surgery, sex, history of febrile convulsion (FC), age at seizure onset, epilepsy duration, seizure frequency, presence of aura, seizure type, number of AEDs used, EEG, MRI, and PET findings, DE insertion, surgical complications, histopathological findings, and seizure outcome at the last follow-up. During the last follow-up, each patient was asked the following question: How satisfied are you with your epilepsy surgery? Or if you had a changes, will you undergo surgery again? The answers were categorized as extremely happy/satisfied and not happy/not satisfied. Data at the last follow-up were collected either from the patients' files, which included the most recent information, or via telephone call.

All patients underwent surgery conducted by the same surgeon using a similar technique. In the last 10 years, ATL has been performed on patients with TLE-HS, and the surgical technique is described in detail elsewhere (15).

Seizure outcome at the last follow-up was categorized as continuous seizure freeness without aura (Engel Ia classification) and relapse. The reasons for this strictest criterion has been reported elsewhere (6,10).

Statistical Analysis

The Statistical Package for the Social Sciences software (version 20.0, IBM Inc., the USA) was used for statistical analysis. The Student's *t*-test was utilized to compare continuous variables. Categorical variables were evaluated using the chi-square test. A P-value of <0.05 was considered statistically significant.

RESULTS

Study Cohort

This study included 64 patients (male/female ratio: 31/33), with a mean age of 32.2 years. The participants did not significantly differ in terms of sex (p=0.80). The mean age at seizure onset was 12 years (range: 6 months to 42 years), and the seizure duration was 19.7 years. Approximately 84.4% of patients had aura, which mainly included increasing epigastric sensation, followed by fear and distress. The mean seizure frequency was 11 per month, and several types of seizures were noted preoperatively. The most common seizure type was symptomatic focal or focal seizure with automatism (n=18 [28.2%]). Moreover, the other main types were complex partial (CP) with automatisms (n=16 [25%]) and CP with secondary generalized tonic-clonic (CP-GTC) seizures (n=6 [9.4%]). Meanwhile, only five (7.8%) patients had automatism. The number of AEDs used varied, and the mean number of AEDs used preoperatively was 2.5 (Table I).

Abnormal discharges in the unilateral temporal plus extra-temporal region (n=36 [56.3%]) was observed on ictal scalp EEG. Moreover, they were observed in the unilateral temporal region (n=13 [20.3%]), bilateral diffuse region (n=4 [6.3%]), and unilateral extra-temporal region (n=3 [4.7%]). Ictal EEG could not facilitate lateralization in seven (10.9%) patients. No pattern was observed in one (1.6%) patient. By contrast, inter-ictal EEG showed abnormal discharges in the temporal plus extra-temporal region (n=29 [45.3%]), unilateral temporal region (n=15 [23.4%]), and unilateral extra-temporal region (n=11 [17.2%]). Three (4.7%) patients had bilateral diffuse discharges. In three (4.7%) patients, inter-ictal EEG could not facilitate lateralization, and another three (4.7%) patients had normal findings.

Preoperatively, all patients underwent head MRI with epilepsy protocol, which is an important part of preoperative diagnostic work-up. In most cases, the MRI (n=61; 95.3%) findings were consistent with TLE-HS. However, three (4.7%) patients had normal MRI findings. In total, 61 (95.3%) patients underwent PET, and various degrees of hypo-metabolism were identified. In 39 (63.9%) patients, the most consistent finding on PET was unilateral temporal hypo-metabolism. In 10 (16.3%) patients, unilateral temporal plus extra-temporal hypo-metabolism was observed on PET. Nine (14.8%) patients presented with hypo-metabolism in the bilateral temporal region. In addition, one (1.6%) patient had hypo-metabolism in the bilateral temporal plus extra-temporal regions. Meanwhile, two (3.3%) patients had normal PET findings. Because of discordant data on seizure semiology and EEG and head MRI findings, 11 (17.2%) patients underwent DE insertion.

Surgery was performed on the right and left sides in 30 (46.9%) and 34 (53.1%) patients, respectively. The surgical side did not significantly differ (p=0.61). Six (9.4%) patients developed surgical complications, and all required re-surgery. Five of six patients had hematoma (n=4, epidural and n=1, subdural). One patient had cerebrospinal fluid leakage from the surgical wound, and none of the patients had further complications postoperatively.

Table I: Statistical Summary of 64 Patients Operated on Temporal Lobe Epilepsy with Hippocampal Sclerosis

Parameters	Before surgery	After surgery	p
Age (yrs)	32.2 ± 9.9		
Gender (M/F)	31/33		0.80
Age at onset (yrs)	12.0 ± 9.0		
Duration (yrs)	19.7 ± 9.5		
FC (yes/no)	23/41		
Aura (yes/no)	54/10	17/47	**0.00001**
Seizure frequency/mo	11.0 ± 16.4	2.25 ± 2.5	**0.00001**
Number of AED	2.5 ± 0.7	1.7 ± 0.8	**0.00001**
Side of surgery (rt/lt)	30/34		0.61
*SF/NSF		37/27	0.21
**Happy/Not happy		61/3	**0.00001**
Follow-up (mo)	58.3 ± 36.1		

*Values are given as mean ± standard deviation. ***SF/NSF:** Seizure-free/Not seizure-free. Seizure-free in this study was accepted as the patients who were continuously seizure-free (even without aura) since surgery.*

***AED:** Anti-epileptic drug; **F:** Female; **FC:** Febrile convulsion; **lt:** Left; **M:** Male; **mo:** Month; **rt:** Right; **yrs:** Years.*

***Happy/Not happy are the answers to the question asked at the last follow-up: How satisfied are you with your epilepsy surgery? (or If you had a change, would you be operated on again?)*

Two types of surgical samples were sent to the pathology department: That is, one was collected from the temporal neocortex and the other from the mesial structures including the hippocampus and para-hippocampus. The histopathological diagnoses related to the cortex were as follows: gliosis (n=27 [42.2%]), FCD (n=26 [40.6%]), and mild malformations of cortical development (mMCD) (n=11 [17.2%]). In 62 (96.9%) patients, HS is the common histopathological diagnosis in the mesial structures. The remaining two (3.1%) patients were diagnosed with gliosis.

The mean follow-up was 53.8 months (4.4 years, range: 6–130 months). At the last follow-up, the mean seizure frequency was 2.25, and there was no significant difference in terms of seizure frequency pre- and postoperatively (p=0.00001). Moreover, 37 (57.8%) patients were seizure-free without aura postoperatively. The remaining 27 (42.2%) patients presented with several types of seizure or aura alone. There was no significant difference in between patients who were seizure-free postoperatively and those who had seizure (p=0.21). The mean seizure type at the follow-up was symptomatic focal seizure (n=7 [10.9%]). Four (6.3%) patients had CP seizures with automatisms, and two (3.1%) patients presented with GTC seizure. Only one (1.6%) patient presented with absence seizure and another one with CP-GTC (3.1%). The postoperative seizure type changed in 3 of 15 patients who had seizure with aura. In total, 17 (26.6%) patients had defined aura at the last follow-up. The number of patients who had aura postoperatively significantly decreased (p=0.00001).

At the last follow-up, 14 (21.9%) patients were drug-free, and 50 (78.1%) patients were still taking AED. The mean number of AED used was 1.7, and the number of patients who used AED significantly decreased postoperatively (p=0.00001). The dosage and number of AED used decreased in 32 (64%) patients, and they did not change in 15 (30%) patients. However, in 3 (6%) patients, either the dosage or the number of AED was increased to control postoperative seizures.

At the last follow-up, 61 (91.3%) patients were extremely happy with the surgical outcome. Of 24 patients who were not seizure-free, 21 (87.5%) were extremely happy postoperatively. However, the satisfaction or happiness of three patients (12.5% of the 24; 4.6% in the whole group) was far from expected. These patients, whose AED dosage or number was increased at the last follow-up, were not seizure-free. The seizure frequency per month decreased significantly in two patients, and it remained constant in one patient.

Young and Adult Patients

Preoperative demographic characteristics and clinical outcomes

The participants were classified into two groups. Tables II and III show the core findings in the young and adult groups. The young group included 16 patients with a mean age of 20.4 ± 1.9 (range: 17–24) years and a male/female ratio of 10/6 (62.5%/37.5%). The adult group comprised 48 patients with a mean age of 36.2 ± 8.1 (range: 25–56) years and a male/female ratio of 21/27 (48.3%/56.2%). There was no significant difference in terms of sex between the two groups (p=0.25). The young group had an extremely early seizure onset than the adult group (p=0.00001). Meanwhile, the adult group had a longer seizure duration than the young group (p=0.001). The proportion of patients with a history of FC did not significantly differ between the young and adult groups (48.8% vs. 33.3%, p=0.55). Approximately 62.5% of patients in the young group and 91.7% in the adult group had self-reported aura preoperatively. Several types of auras were noted, which included increasing epigastric sensations, awful feeling in the ear, and auras of the taste and smell. In the young and adult groups, epigastric sensation (18.8% vs. 20.8%) was the most common type of aura, followed by a feeling of fear. Distress and nausea were the other common types of auras in adults. The type of aura did not significantly differ between the two groups (p=0.22). The mean seizure frequency did not significantly differ between the young and adult groups (10.8 ± 10.6 vs. 11.1 ± 18.1 per month, p=0.93). Different types of seizures including CP, CP-GTC, CP with automatisms, simple partial (SP), SP seizures with automatisms, and GTC seizures were noted. The most common types of seizures in young patients were CP with automatisms (n=5, 31.2%), focal with automatisms (n=3, 18.8%), and CP (n=2, 12.5%). Symptomatic seizures with automatisms were observed in 15 (31.2%) patients, CP seizures with automatisms in 11 (22.9%), focal seizures in 6 (12.5%), and CP seizures with secondary generalization in 5 (10.4%). Furthermore, GTC seizures alone were noted in the young and adult groups. However, the incidence was low. The seizure type did not significantly differ between the young and adult groups (p=0.53). There was no significant difference in the mean number of AED used between the young and adult groups (0.8 ± 0.7 [range: 2–4] vs. 2.4 ± 0.6 [range: 1–4], p=0.12) (Table II).

Preoperative radiological outcomes

All patients underwent MRI. In the young group, MRI revealed the common findings of TLE-HS. These included hippocampal atrophy with or without temporal lobe atrophy and hyper-intense signal in the mesial temporal structures, which are best visualized on fluid-attenuated inversion recovery and T2-weighted imaging. However, 45 (93.8%) adult patients had common MRI findings, and three (6.2%) patients had normal results. There were no significant differences in terms of MRI findings between the two groups (p=0.56). PET is another important routine diagnostic method in TLE-HS. The proportion of patients in the young and adult groups who underwent PET was almost similar (15 [93.8%] vs. 46 [95.8%], p=0.58). PET studies showed hypo-metabolism in the unilateral temporal plus extra-temporal region in 7 (46.7%) young patients, unilateral temporal region in 7 (46.7%), and bilateral temporal plus extra-temporal region in 1 (6.7%). Some adult patients had hypo-metabolism in the unilateral temporal region (n=32 [69.6%]), bilateral temporal region (n=9 [19.6%]), and unilateral temporal plus extra-temporal region (n=3 [6.5%]). Meanwhile, two (2.1%) patients had a normal metabolism. The focal hypo-metabolism on PET was significantly higher in adult than in young patients, and hypo-metabolism was more significantly diffused in young than in adult patients (p=0.001) (Table III).

Preoperative electrophysiological outcomes

All patients underwent scalp EEG to out epileptogenic zone. On scalp ictal EEG, abnormal electrical discharges in a single temporal lobe was not common in the young and adult groups. In young patients, the abnormal discharges were generally spike-and-wave or sharp waves in the unilateral temporal plus extra-temporal region (n=10 [62.5%]) and the unilateral temporal region (n=3 [18.8%]). Scalp ictal EEG could not lateralize the pathological side in three (18.8%) patients. In adults, abnormal discharges were observed in the unilateral temporal plus extra-temporal region (n=26 [54.2%]), unilateral temporal region (n=10 [20.8%]), bilateral diffuse region (n=4 [8.3%]), and unilateral extra-temporal region (n=3, [6.2%]). Scalp ictal EEG could not lateralize the side in four (8.3%) patients, and no pattern was noted in one (2.1%) patient. Hence, there was no statistically significant difference in scalp ictal EEG findings between the two groups (p = 0.54). In young and adult patients, scalp inter-ictal EEG showed abnormal electrical discharges in the following structures: unilateral temporal plus extra-temporal region (9 [56.2%] vs. 20 [41.7%]), unilateral temporal region (4 [25%] vs. 11 [22.9%]), unilateral extra-temporal (2 [12.5%] vs. 9 [18.8%]), and diffuse bilateral hemisphere (1 [6.2%] vs. 2 [4.2%]). In addition, in three (6.2%) patients from the adult group, scalp inter-ictal EEG showed no lateralization. Meanwhile, another three (6.2%) patients had normal results. Regarding cerebral lobe involvement based

Table II: Summary of Some Demographic and Follow-Up Data of the Two Groups Operated on Temporal Lobe Epilepsy With Hippocampal Sclerosis

Parameters	Before surgery		After surgery	
	Young	**Adult**	**Young**	**Adult**
Age (yrs)	20.4 ± 1.9	36.2 ± 8.1		
Gender (M/F)	10/6	21/27		
Age at onset (yrs)	6.4 ± 4.6	13.8 ± 9.3		
Duration (yrs)	14.2 ± 5.3	21.5 ± 9.9		
FC (yes/no)	7/9	16/32		
Aura (yes/no)	10/6	44/4	3/13	14/34
Sz frequency/mo	10.8 ± 10.6	11.1 ± 18.1	3.5 ± 3.5	2.0 ± 2.5
AED (yes/no)	16/0	48/0	11/5	39/9
Number of AED	2.8 ± 0.7	2.4 ± 0.6	1.6 ± 1.2	1.7 ± 0.7
PET (yes/no)	15/1	46/2		
DE (yes/no)	1/15	10/38		
Surg side (rt/lt)	7/9	23/25		
Comp (yes/no)			2/14	4/44
Follow-up (mo)			56.1 ± 35.8	59.1 ± 36.5
*SF/NSF			11/5	26/22
**Happy/Not happy			15/1	46/2

Values are given as mean ± standard deviation.
***SF/NSF:** Seizure-free/Not seizure-free. Seizure-free in this study was accepted as the patients who were continuously seizure-free (even without aura) since surgery. **Happy/Not happy are the answers to the question asked at the last follow-up: How satisfied are you with your epilepsy surgery? (or If you had a change, would you be operated on again?*
***AED:** Anti-epileptic drug; **Comp:** Complication; **DE:** Depth electrode; **F:** Female; **FC:** Febrile convulsion; **lt:** Left; **M:** Male; **mo:** Month; **PET:** Positron emission tomography; **rt:** Right; **Surg:** Surgical; **Sz:** Seizure; **yrs:** Years.*

on abnormal electrical discharges on scalp inter-ictal EEG, no significant difference was found between the two groups (p=0.70). In this series, because of discordant data between the scalp EEG and radiological studies, invasive EEG studies with DE insertion under the guidance of neuronavigation were performed on one (6.2%) young and 10 (20.8%) adult patients to identify the exact side and/or site of the epileptogenic zones. The need for invasive studies did not significantly differ between the two groups (p=0.26) (Table III).

Surgical complications and histopathological results

All patients underwent ATL. Surgical resections were performed on the right and left temporal lobes in seven (43.8%) and nine (56.2%) young patients, respectively. In total, 23 (47.9%) and 25 (52.1%) adult patients underwent right and left temporal resections, respectively. There were no significant differences in terms of the side of surgery between the two groups (p=0.77). Moreover, two (12.5%) young and four (8.3%) adult patients developed surgical complications, and all required re-surgery. The complication rates did not significantly differ between the young and adult groups (p=0.63). HS was the most common histopathological diagnosis between the two groups. Mesial temporal structures were diagnosed as HS in all young (100%) and in 46 adult (95.8%) patients and in 2 patients gliosis (4.2%) in the mesial temporal area was the pathological substrate in adults. By contrast, the temporal cortices had different pathological diagnosis. Gliosis (6 [37.5%] vs. 21 [43.8%]), FCD (6 [37.5%] vs. 20 [41.7%]), and mMCD (4 [25%] vs. 7 [14.6%]) were observed in the temporal cortices of the young and adult groups. The histopathological diagnosis was similar between the two groups with respect to the mesial temporal structures (p=0.40) and the temporal cortices (p=0.63) (Table III).

Follow-up outcomes

The mean follow-up time between the young and adult groups did not significant differ (56.1 ± 35.8 [16–129] vs. 59.1 ± 36.5 [range: 6–130] months, p=0.78). The proportion of patients who were seizure-free at the last follow-up did not significantly differ between the young and adult groups (11 [68.8%] vs. 26 [54.2%], p=0.38). Further, 5 (31.2%) young and 22 (45.8%) adult patients experienced seizure once or more. The mean

Table III: Summary of Core Findings of Radiological, Electrophysiological and Pathological Studies in the Two Groups Operated on Temporal Lobe Epilepsy with Hippocampal Sclerosis

Parameters	Before surgery		After surgery	
	Young	Adult	Young	Adult
MRI				
Exp find/Normal	16/0	45/3		
PET				
UT-ET/UT/BT/Normal	7/7/1	3/32/9/2		
Ictal EEG				
UT-ET/NoL/UT	10/3/3	26/4/10		
Inter-ictal EEG				
UT-ET/NoL/UT	9/0/4	20/3/11		
Follow-up EEG				
UT/UT-ET/Normal			3/2/10	18/5/21
Pathology: HC+PHC				
HS/Gliosis			16/0	46/2
Pathology: Cortex				
Gliosis/FCD/mMCD			6/6/4	21/20/7

BT: *Bilateral temporal;* ***EEG:*** *Electroencephalography;* ***Exp Find:*** *Expected findings related to temporal lobe epilepsy;* ***FCD:*** *Focal cortical dysplasia;* ***HC+PHC:*** *Hippocampus + para-hippocampus;* ***HS:*** *Hippocampal sclerosis;* ***mMCD:*** *Mild malformation of cortical development;* ***MRI:*** *Magnetic resonance imaging;* ***NoL:*** *No lateralization;* ***PET:*** *Positron emission tomography;* ***UT-ET:*** *Unilateral temporal and extra-temporal;* ***UT:*** *Unilateral temporal.*

seizure frequency did not significantly differ between the young and adult groups (3.5 ± 3.5 vs. 2.0 ± 2.5 per month, p=0.46). There was no significant difference in terms of the proportion of patients with postoperative aura between the young and adult groups (3 [18.8%] vs. 14 [29.2%], p=0.52). The proportion of patients who were drug-free at the last follow-up did not significantly differ between the young and adult groups (5 [31.2%] vs. 9 [18.8%], p=0.31). Most patients in both groups were on AED therapy irrespective of seizure freeness. Eleven (68.8%) young and 39 (81.2%) adult patients were still on AED therapy at the last follow-up. The mean numbers of AED used did not significantly differ between the young and adult groups (1.6 ± 1.2 vs. 1.7 ± 0.7, p=0.59). In total, 8 (72.7%) young and 24 (61.5%) adult patients had decreased dosage or number of AEDs used during follow-up. Further, 2 (18.2%) young and 13 (33.3%) adult patients had a similar dosage and/or number of AEDs used pre- and postoperatively. However, one (9.1%) young and two (5.1%) adult patients had an increased dosage and/or number of AED used. Surgery was beneficial for the two groups. However, the proportion of patients who had decreased dosage and/or number of AEDs used at the last follow-up did not significantly differ between the two groups (p=0.59) (Tables I, II). In total, 10 (62.5%) young and 21 (32.8%) adult patients had normal scalp EEG results at the final follow-up. In the young group, slow but abnormal discharges were observed in the unilateral temporal region (n=3 [18.8%]), unilateral temporal plus extra-temporal region (n=2 [12.5%]), and bi-temporal region (n=1 [6.2%]). Meanwhile, in the adult group, these discharges were observed in the unilateral temporal region (n=18 [37.5%]), unilateral temporal plus extra-temporal region (n=5 [10.4%]), and unilateral extra-temporal region (n=2 [4.2%]). Two (4.2%) adult patients had bi-temporal slow waves. The postoperative scalp EEG findings did not significantly differ between the two groups (p=0.56). The scalp EEG results at the last follow-up indicated that there was a tendency to decline in diffuse bi-hemispheric involvement and an incline to involve single lobe or one side of the cerebrum (Table III).

The surgical outcome was evaluated using the following question: How satisfied are you with the epilepsy surgery? Or if you had a change, will you undergo re-surgery? A significant proportion of patients in the young and adult groups were extremely happy or satisfied with the surgical outcomes. However, the proportion of patients who were satisfied with the surgical outcome did not significantly differ between the young and adult groups (15 [93.8%] vs. 46 [95.8%], p=0.73). One (6.2%) young and two (4.2%) adult patients were not happy with the surgical outcome. In addition, the seizure frequency decreased significantly postoperatively (Table II).

DISCUSSION

This study is one of the rarely published series on TLE-HS. Its main findings were are as follows: First, TLE-HS surgery was extremely safe with a low complication rate and extremely effective with a high continuous seizure-free rate. Second, seizure semiology and electrophysiological and radiological findings were similar between the young and adult groups. Third, HS in the mesial temporal region was the most common pathological diagnosis, and FCD/mMCD in the temporal neocortex is a frequent diagnosis in the two groups. Fourth, the continuous seizure-free and drug-free rates were similar between the two groups. Fifth, the satisfaction rate of both groups was extremely high.

The sample size of the current study might be small or insufficient. Thus, a solid conclusion could not be drawn. However, the number of patients with TLE-HS proceeding from diagnostic studies to surgical resection is decreasing. The number of patients who are reluctant to undergo EEG, an invasive procedure, is increasing primarily because of exaggerated risk perception (4,6,8). Moreover, the decreasing rate of resective surgery for TLE-HS is attributed to the consideration of this entity as easy-to-treat group and be operated in other not-tertiary centers. Notably, comparing and discussing seizure outcomes are extremely challenging because there is no common consensus between centers regarding the use of a similar classification scheme. There are two available seizure outcome scales. However, that they are not sufficient for assessing each patient with postoperative seizures such as single seizure after AED withdrawal and seizure occurrence 2 years postoperatively with seizure freeness thereafter (6,9,10). In this study, for simplicity, seizure outcome was classified into continuous seizure freeness without aura and relapse (6). Thus, seizure freeness without aura indicates that the epileptogenic zone has already been included in the resected tissues. This type of seizure outcome may lead to a perception that surgery is correlated with a less favorable seizure outcome. However, patients who were seizure-free without aura postoperatively, but not those with a favorable seizure outcome (Engel I and II classification), were included in the analysis.

Our research did not show significant differences in terms of pre-surgical, histopathological, and post-surgical outcomes between the young and adult groups. This result is not in accordance with that of other studies that mainly included different age groups with diverse pathologies causing TLE (5,8,13). In our series, none of the patients aged under 17 years old had different etiologies and electrophysiological and radiological features. As expected and based on previous studies, both groups had a history of FC and typical aura such as increasing epigastric sensations (3,4,15). However, we did not frequently observe GT or GTC seizures in the young and adult groups, which differs from other studies in the literature. In another study, up to 30% of older children experienced GT seizures (13,14). The difference is attributed to variations in the inclusion criteria. In our research, the young group was more likely to have more frequent CP seizures with automatism than the adult group.

In our study, head MRI findings including atrophy of the temporal lobe and hyper-intensity in the mesial structures were expected. Moreover, there were no significant differences in head MRI findings between the young and adult groups, which is similar to previous studies (3,4-6,8,13). By contrast, focal hypo-metabolisms on PET were significantly more common in adult than in young patients. However, the proportion of young patients with diffuse hypo-metabolisms was significantly higher than that of adult patients in this series. Extensive hypo-metabolisms have been noted on PET in TLE-HS, which can pose diagnostic challenges in younger patients (2,12). In a previous study, hypo-metabolisms in the temporal lobe in TLE-HS may be structural rather than functional. In addition, seizure outcome is not as high as in those with more focal hypo-metabolisms on PET, and this should be discussed with patients preoperatively (2).

Based on previous and the current studies, more focal ictal and inter-ictal scalp EEG findings is very difficult in TLE-HS (3,4,5,8,13,14). Commonly, scalp EEG findings are more diffuse and complex, which pose a risk for diagnosing or localizing and/or lateralizing temporal lobe seizure onset. Some studies have shown that focal inter-ictal EEG abnormalities are more commonly observed in adolescents than in young children. However, some revealed more significant focal inter-ictal EEG abnormalities in adults (13,14). Notably, scalp EEG findings, particularly ictal EEG, have a limited value (7). In our study, most patients in the young and adult groups had diffuse ictal and inter-ictal EEG abnormalities in the unilateral temporal plus extra-temporal region. However, the findings did not significantly differ. However, diffuse EEG abnormalities were more frequently noted in young than in adult patients. Our scalp ictal and inter-ictal EEG findings in TLE-HS are in accordance with those in the current literature. Moreover, temporal lobe seizure onset was easier to identify using PET and invasive EEG studies. Thus, these methods have become the building blocks in epilepsy diagnostic work-up.

Epilepsy surgery is extremely safe with a low complication rate (15,17). In the current literature, the surgical complications rates ranged from 0% to 16%, and our complication rate (9.4%) was within this range (1,11,15,17). The placement of invasive electrodes may also increase the complication rate particularly in young patients. However, the rate is extremely low (15). In our study, all patients who had surgical complications (one patient after DE insertion) underwent re-surgery. Nevertheless, there was no significant difference in the surgical complication rates between young and adult patients. Thus, ATL is extremely safe and effective considering that the temporal neocortex may have a dual pathology such as FCD, which cannot be observed on preoperative MRI. Further, ATL, rather than selective amygdalohippocampectomy, has been performed on patients with TLE-HS during the last two decades.

HS in the mesial temporal region is the most common pathological finding in the young and adult groups. Moreover, cortical developmental abnormalities were noted in both groups. Nevertheless, the pathological findings did not significantly differ. Our results are in accordance with those of previous studies on young patients. However, as suggested, similar to young adults or children, a higher proportion of adult patients with TLE-HS may have cortical developmental malformations such as FCD and mMCD (2,3,8,13).

In the current study, the young and adult groups had a longer follow-up. The continuous seizure-free rate of the cohort was 57.8%, and the drug-free rate at the last follow-up was 21.9%. The seizure-free rate in this study might be lower than that in previous larger series. However, we included patients who were continuously seizure-free without aura and those with TLE-HS alone (5,8). In general, previous studies have shown favorable outcomes (Engel I + II classification). Furthermore, some report showed that aura was not a sign of relapse (3,13). In this report, surgery was beneficial for the young and adult groups. However, the outcomes did not significantly differ. The seizure-free rates at the last follow-up were 68.8% and 54.2% in the young and adult groups, respectively. Our findings are in accordance with those in the literature, which showed that seizure freeness is more frequent in younger patients, and early surgery is recommended (3,5,8,13). Similar to previous literature, AED discontinuation is more common in younger than in adult patients. However, our study did not show significant differences in the AED discontinuation rates (31.2% vs. 18.8%) (5,8). Most patients in both groups had normal scalp ictal and inter-ictal EEG findings. Meanwhile, patients who had EEG abnormalities had more unilateral temporal slow waves postoperatively (3,4,13).

This study did not include data on post-surgical QoL. However, the effect of surgical outcomes on patient perception was evaluated using a sing/simple question. A significantly higher proportion of patients in the young and adult groups were extremely happy with the surgical outcomes. Nearly 94% of young and 96% of adult patients were happy or satisfied with the surgical outcomes. Moreover, 87.5% of patients who had seizure at the follow-up period were happy. Therefore, not only seizure freeness but also a significantly lower seizure frequency may be sufficient to make the patients happy or satisfied. Thus, seizure freeness is not the final aspect of happiness. Moreover, evaluation in terms of several measures should be considered when determining surgical outcome.

Study Limitations

The current study had several limitations. First, it was a retrospective clinical-based study that included a limited number of patients who underwent TLE-HS surgery. Second, this study did not represent the full spectrum of patients with TLE.

CONCLUSION

Epilepsy surgery is extremely effective in both young and adult patients with TLE-HS. The two groups have similar pre-surgical, histopathological, and post-surgical outcomes and a high seizure freeness and satisfaction rate.

AUTHORSHIP CONTRIBUTION

Study conception and design: SNY, TT
Data collection: SCC, TAK
Analysis and interpretation of results: TSK, TT
Draft manuscript preparation: SCC, RK
Critical revision of the article: SCC, TT
Other (study supervision, fundings, materials, etc...): TAK, SNY
All authors (SCC, TAK, TSK, RK, SNY, TT) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Ahmedov ML, Korkmaz TS, Kemerdere R, Yeni SN, Tanriverdi T: Surgical and neurological complications in temporal lobe epilepsy surgery in modern era. Surg Neurol Int 9:134, 2018
2. Alizada O, Akgun E, Akgun MY, Kemerdere R, Yeni SN, Tanriverdi T: What happens to temporal hypometabolism contralateral to side of surgery in patients with bilateral temporal hypometabolism? Clin Neurol Neurosurg 178:7-12, 2019
3. Asadi-Pooya AA, Sperling MR: Age at onset in patients with medically refractory temporal lobe epilepsy and mesial temporal sclerosis: Impact on clinical manifestations and postsurgical outcome. Seizure 30:42-45, 2015
4. Ayas S, Kurtish SY, Tanriverdi T, Yeni SN: Evaluation of patients with late-onset and medically refractory temporal lobe epilepsy with mesial temporal sclerosis. Clin Neurol Neurosurg 198:106209, 2020
5. Barba C, Cossu M, Guerrini R, Di Gennaro G, Villani F, De Palma L, Grisotto L, Consales A, Battaglia D, Zamponi N, d'Orio P, Revay M, Rizzi M, Casciato S, Esposito V, Quarato PP, Di Giacomo R, Didato G, Pastori C, Pavia GC, Pellacani S, Matta G, Pacetti M, Tamburrini G, Cesaroni E, Colicchio G, Vatti G, Asioli S, Caulo M, Marras CE, Tassi L: Temporal lobe epilepsy surgery in children and adults: A multicenter study. Epilepsia 62(1):128-142, 2021
6. Bien CG, Raabe AL, Schramm J, Becker A, Urbach H, Elger CE: Trends in presurgical evaluation and surgical treatment of epilepsy at one centre from 1988-2009. J Neurol Neurosurg Psychiatry 84:54-61, 2013
7. Brockhaus A, Elger CE: Complex partial seizures of temporal lobe origin in children of different age groups. Epilepsia 36: 1173-1181, 1995
8. Cloppenborg T, May TW, Blümcke I, Fauser S, Grewe P, Hopf JL, Kalbhenn T, Polster T, Schulz R, Woermann FG, Bien CG: Differences in pediatric and adult epilepsy surgery: A comparison at one center from 1990 to 2014. Epilepsia 60: 233-245, 2019
9. De Tisi J, Bell GS, Peacock JL, McEvoy AW, Harkness WF, Sander JW, Duncan JS: The long-term outcome of adult epilepsy surgery, patterns of seizure remission, and relapse: A cohort study. Lancet 378:1388-1395, 2011
10. Engel J, JR, Van Ness PC, Rasmussen TB, Ojemann LM: Outcome with respect to epileptic seizures. In: Engel J Jr, ed. Surgical Treatment of the Epilepsies. New York, NY: Raven Press, 1993:609-621

11. Georgiadis I, Kapsalaki EZ, Fountas KN: Temporal lobe resective surgery for medically intractable epilepsy: a review of complications and side effects. Epilepsy Res Treat 2013: 752195, 2013
12. Joo EY, Lee EK, Tae WS, Hong SB: Unitemporal vs. bitemporal hypometabolism in mesial temporal lobe epilepsy. Arch Neurol 61: 1074-1078, 2004
13. Lee YJ, Kang HC, Bae SJ, Kim HD, Kim JT, Lee BI, Heo K, Jang JW, Kim DS, Kim TS, Lee JS: Comparison of temporal lobectomies of children and adults with intractable temporal lobe epilepsy. Childs Nerv Syst 26: 177-183, 2010
14. Mohamed A, Wyllie E, Ruggieri P, Kotagal P, Babb T, Hilbig A, Wylie C, Ying Z, Staugaitis S, Najm I, Bulacio J, Foldvary N, Lüders H, Bingaman W: Temporal lobe epilepsy due to hippocampal sclerosis in pediatric candidates for epilepsy surgery. Neurology 56: 1643-1649, 2001
15. Olivier A, Boling WW, Tanriverdi T. Techniques in Epilepsy Surgery: the MNI Approach. 1st ed. United Kingdom: Cambridge University Press; 2012
16. Spencer S, Huh L: Outcome of epilepsy in adults and children. Lancet Neurol 7: 525-537, 2008
17. Tanriverdi T, Ajlan A, Poulin N, Olivier A: Morbidity in epilepsy surgery: an experienced based on 2449 epilepsy surgery procedures from a single institution. J Neurosurg 110: 1111-1123, 2009
18. Tanriverdi T, Olivier A, Poulin N, Andermann F, Dubeau F: Long-term seizure outcome after mesial temporal lobe epilepsy surgery: cortico-amygdalohippocampectomy versus selective-amygdalohippocampectomy. J Neurol Surg 108: 517-524, 2008
19. Tanriverdi T, Poulin N, Olivier A: Life 12 years after temporal lobe epilepsy surgery: a long-term, prospective clinical study. Seizure 17: 339-349, 2008
20. Thom M, Eriksson S, Martinian L, Caboclo LO, McEvoy AW, Duncan JS, Sisodiya SM: Temporal lobe sclerosis associated with hippocampal sclerosis in temporal lobe epilepsy: neuropathological features. J Neuropathol Exp Neurol 68: 928-938, 2009
21. Wiebe S, Blume WT, Girvin JP, Eliasziw M: A randomized controlled trial of surgery for temporal lobe epilepsy. N Engl J Med 345: 311-318, 2001