A study of medial and lateral temporal lobe epilepsy based on stereoelectroencephalography

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Abstract

Background: Patients with temporal lobe epilepsy (TLE) originating from different seizure onset zones had distinct electrophysiological characteristics and surgical outcomes. In this study, we aimed to investigate the relationship between the origin and prognosis of TLE, and the stereoelectroencephalography (SEEG) features.

Methods: Thirty patients with TLE, who underwent surgical treatment in our functional neurosurgery department from January 2016 to December 2017, were enrolled in this study. All patients underwent anterior temporal lobectomy after an invasive pre-operative evaluation with SEEG. Depending on the epileptic focus location, patients were divided into those with medial temporal lobe seizures (MTLS) and those with lateral temporal lobe seizures (LTLS). The Engel classification was used to evaluate operation effectiveness, and the Kaplan-Meier analysis was used to detect seizure-free duration.

Results: The mean follow-up time was 25.7 ± 4.8 months. Effectiveness was 63.3% for Engel I ($n = 19$), 13.3% for Engel II, 3.3% for Engel III, and 20.0% for Engel IV. According to the SEEG, 60.0% ($n = 18$) had MTLS, and 40.0% ($n = 12$) had LTLS. Compared with the MTLS group, the operation age of those with LTLS was significantly greater (26.9 ± 6.9 *vs.* 29.9 ± 12.5 years, $t = -0.840$, $P = 0.009$) with longer epilepsy duration (11.9 ± 6.0 *vs.* 17.9 ± 12.1 years, $t = -1.801$, $P = 0.038$). Patients with MTLS had a longer time interval between ictal onset to seizure (67.3 ± 59.1 s *vs.* 29.3 ± 24.4 s, $t = 2.017$, $P = 0.008$). The most common SEEG ictal pattern was a sharp/spike-wave rhythm in the MTLS group (55.6%) and low-voltage fast activity in the LTLS group (58.3%). Compared with the LTLS group, patients with MTLS had a more favorable prognosis (41.7% *vs.* 77.8%, $P = 0.049$). Post-operative recurrence was more likely to occur within three months after the operation for both groups, and there appeared to be a stable long-term outcome.

Conclusion: Patients with MTLS, who accounted for three-fifths of patients with TLE, showed a more favorable surgical outcome.

Keywords: Epilepsy; Stereoelectroencephalography; Surgical outcome; Temporal lobe

Introduction

Temporal lobe epilepsy (TLE) is a type of epilepsy that originates unilaterally or bilaterally from the temporal lobe structure and is the most common form of drug-refractory epilepsy with an incidence of 60% to 80%.[1,2] Hippocampal sclerosis (HS) is a typical imaging feature of TLE, especially in mesial TLE.[3] However, not all patients with TLE have significant HS, leading to the dilemma of identifying TLE, especially when patients show negative magnetic resonance imaging (MRI) scans.[4] Therefore, for suspected TLE in which the epileptogenic zone could not be located by non-invasive evaluations, intracranial electrodes are recommended, including subdural electrodes or stereoelectroencephalography (SEEG) based on the anatomo-electro-clinical presentation.[5,6] Compared with subdural electroencephalogram (EEG), SEEG is more minimally invasive and able to monitor deep structures, such as the hippocampus, amygdala, and insula.[7-9] Depending on the location of the epileptic focus and the depth of the electrodes, TLE may be divided into numerous subdivisions, from the mesiotemporal subtype to the widely extended temporal plus subtype.[10] Mesial temporal lobe epilepsy (MTLE) is the main type of TLE, accounting for 70%.[11,12] It has been reported that epilepsy with distinct origins has different SEEG characteristics, such as low-voltage fast activity, spike-wave activity, periodic spikes,[13,14] and different ictal onset patterns influence post-operative prognosis.[11,15-17] Few studies have reported the clinical and SEEG features of MTLE and

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lateral temporal epilepsy. In this study, the clinical data, EEG onset patterns, and the long-term outcome of 30 patients with drug-refractory TLE, who were classified with either mesial or lateral temporal lobe structures via SEEG, were analyzed retrospectively.

Methods

Ethics

This study was approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University, China, according to the *Declaration of Helsinki*. A written informed consent was obtained from all patients and their relatives in the study.

Clinical characteristics of patients

Thirty patients with TLE were enrolled from the Functional Neurosurgery Department, Xuanwu Hospital, Capital Medical University, from January 2016 to December 2017. Inclusion criteria included: (1) the patients had seizures during SEEG recording; (2) the patients underwent temporal resection surgery, and (3) the time of follow-up was >1 year after the operation. There were 13 men and 17 women. The age of onset was 1–31 (13.8 ± 8.2) years. The duration of epilepsy was 3–46 (14.3 ± 9.2) years, and the operation age was 10–52 (28.1 ± 9.4) years. The mean pos-operative follow-up time was 25.7 ± 4.8 (12–37) months.

Pre-operative evaluation and pathological findings

All patients underwent conventional MRI, including a spin-echo sequence with a T1-weighted phase, T2-weighted phase, and an oblique coronal fluid attenuation inversion perpendicular to the long axis of the hippocampus (fluid-attenuated inversion-recovery) sequence. All patients were further monitored by video EEG with the international standard 10 to 20 system, and interictal and ictal EEG were recorded with at least three clinical seizures. In addition, some patients underwent magnetoencephalography and positron emission tomography/MRI examinations. After a comprehensive evaluation, localization of the epileptic foci was defined according to clinical symptoms, EEG, and imaging examination.

For patients whose epileptogenic focus could not be identified by the above non-invasive examinations, stereotactic deep electrodes were implanted. The intracerebral multiple contact electrodes were semirigid platinum/iridium with contacts between 10 and 16. They were 2 mm in length, 0.8 mm in diameter, and 1.5 mm apart. The anatomical target exploration was performed according to standard stereotactic surgery procedures using the Cosman-Roberts-Wells frame (Radionics, Burlington, MA, USA). A computed tomography (CT) scan (Siemens 1.5 T, Sonata, Germany) was acquired, and image fusion was performed with the pre-operative T1 MRI sequences (Siemens 3.0 T, Sonata) using the NeuroGuide system (STEALTH Framelink, Medtronic, Inc., Minneapolis, MN, USA). The magnetic resonance venography and magnetic resonance angiography were additionally obtained and fused to avoid major vessel injury in the design of the electrode trajectories. The electrodes were implanted one by one using an oblique approach. A CT scan was performed immediately after electrode implantation to check for post-operative complications, and CT-scan/pre-implant MRI data fusion was performed to accurately check the anatomical location of each contact along the electrode trajectory.

The interictal and ictal SEEG were recorded, and three clinical seizures were recorded. The electrocorticography monitoring was performed intraoperatively to determine the extent of temporal cortex resection. Pathological examinations were performed on the excised brain tissue.

SEEG data analysis

Analysis of the interictal and ictal SEEG characteristics was performed to determine ictal patterns and the location of the electrode contacts. Depending on the seizure onset location, patients were divided as having either mesial or lateral TLE.

Efficacy assessment

Post-operative follow-up was 12 to 37 months, and efficacy was evaluated according to the Engel classification[18]: level I, those who were seizure-free, had the only aura of seizures, or seizures due to the discontinuation of antiepileptic drugs; level II, those whose seizure frequency was reduced by 90% or experienced only night-time episodes; level III, those whose seizure frequency was reduced by 75% to 90%; and level IV, those whose seizure frequency was reduced by <75%, had no significant improvement, or even increased seizure frequency.

Statistical methods

SPSS 21.0 statistical software package (IBM, Chicago, IL, USA) was used for statistical analysis of the data. The continuous variable was described as mean ± standard deviation, and a two-sample *t*-test was selected to compare the difference. The Kaplan-Meier analysis was used to compare differences among the different subgroups post-operation. A value of $P < 0.05$ indicated that the difference was statistically significant.

Results

SEEG characteristics

The average number of electrodes was 6 (2–8) per patient, and the average electrode contacts were 85 (32–114). Among the 30 patients, 15 were implanted with bilateral electrodes, six with left electrodes, and nine with right electrodes. A total of 151 seizures were recorded, with an average of five seizures per patient. Nineteen patients had complex partial seizures, and 11 patients had secondary generalized tonic-clonic seizures. There were five ictal onset patterns for SEEG: low-amplitude fast wave rhythm ($n = 11$, 36.7%), sharp wave rhythm ($n = 13$, 43.3%), spike and ware wave rhythm ($n = 3$, 10.0%), rhythmic sharp wave ($n = 2$, 6.7%), and slow-wave rhythm ($n = 1$, 3.3%). The mean time from the ictal onset of SEEG to the onset of clinical symptoms was 52.9 ± 40.7 s (3.5–194.5 s), and the average duration of symptoms was 80.4 ± 19.6 s (24.0–195.0 s).

Post-operative follow-up results

The mean post-operative follow-up time was 25.7 ± 4.8 months, and 19 (63.3%) cases were Engel level I, four (13.3%) cases were Engel level II, one (3.3%) case was Engel level III, and six (20.0%) cases were Engel level IV. The recurrence of seizures was more likely to occur within 3 months after the operation with a rate of 37.3%, as shown in Figure 1.

Comparison of clinical data between patients with MTLS and LTLS

The mesial and lateral temporal lobe origins were determined depending on the detection of the initial recording of the SEEG signal from the electrode contact. There were 18 (60.0%) patients with MTLS and 12 (40.0%) with LTLS. The comparison of the two groups showed that the operation age was older ($P = 0.009$) and the epilepsy duration was longer ($P = 0.038$) in patients with LTLS. Whereas, patients with MTLS had a longer duration from the onset of SEEG to the appearance of clinical symptoms ($P = 0.008$), as shown in Table 1.

The most common SEEG ictal onset patterns in patients with MTLS was sharp/spike-wave rhythm (55.6%), followed by the low-amplitude fast wave rhythm (22.2%). In patients with LTLS, the low-amplitude fast wave rhythm (58.3%) and sharp/spike rhythm (25.0%) were the most common.

The surgical results in patients with MTLS showed 14 for Engel level I (77.8%), two for Engel level II (11.1%), and two for Engel level IV (11.1%). In patients with LTLS, the results showed five for Engel level I (41.7%), two for Engel level II (16.7%), one for Engel level III (8.3%), and four for Engel level IV (33.3%). The percentage of patients with MTLS free of seizures was higher than those with LTLS ($P = 0.049$), as shown in Figure 2. The 95% confidence interval was 0.768–5.232.

The pathological results of the 30 patients showed that 13 (72.2%) patients with MTLS had HS with focal cortical dysplasia and that five patients (27.8%) did not. In the LTLS group, one patient (8.3%) had HS, whereas 11 patients (91.7%) did not.

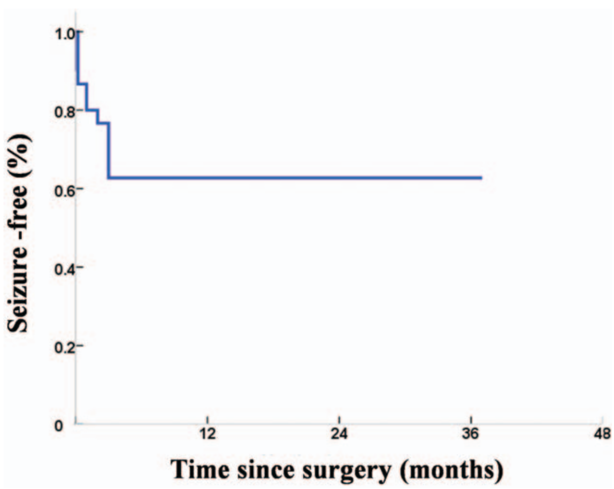

Figure 1: Post-operative Kaplan-Meier analysis for all patients.

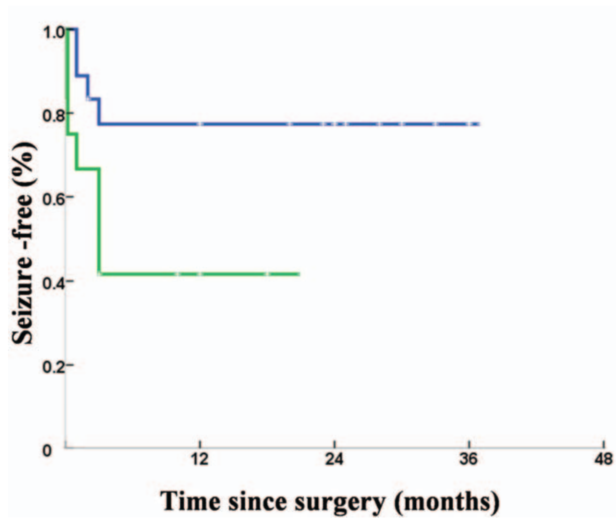

Figure 2: Kaplan-Meier analysis of patients with medial temporal lobe epilepsy and temporal lobe neocortical epilepsy. The blue line represented the MTLS group, and the green line represented the LTLS group ($P = 0.049$). LTLS: Lateral temporal lobe seizures; MTLS: Medial temporal lobe seizures.

Table 1: Comparison of clinical data between patients with medial temporal lobe and lateral temporal lobe origins.

Parameters	Medial temporal lobe ($n = 18$)	Lateral temporal lobe ($n = 12$)	t	P
Gender (M/F)	8/10	5/7		
Age of onset (years)	15.0 ± 7.2	12.0 ± 9.6	0.978	0.109
Age of surgery (years)	26.9 ± 6.9	29.9 ± 12.5	−0.840	0.009
Couse of disease (years)	11.9 ± 6.0	17.9 ± 12.1	−1.801	0.038
The time from the onset of SEEG to the onset of symptoms (s)	67.3 ± 59.1	29.3 ± 24.4	2.017	0.008
Symptoms appear until the end of discharge (s)	87.0 ± 45.3	69.5 ± 22.5	1.189	0.086
Follow-up time (months)	27.7 ± 8.0	22.7 ± 6.0	1.872	0.239

Data are presented as *n* or mean ± standard deviation M: Male; F: Female; SEEG: Stereoelectroencephalography.

Discussion

In this study, TLE was divided into MTLS and LTLS depending on the seizure onset zone determined by SEEG. Of the 30 patients, 60.0% were classified into the MTLE group and 40% were classified into the LTLE group. There was a significant difference in the SEEG patterns and long-term post-operative outcomes between the two subgroups. The sharp/spike-wave rhythms were more common in patients with MTLS, while low-amplitude fast wave rhythms were more common in those with LTLS. A longer duration from the onset of SEEG discharges to the presence of clinical symptoms was detected in patients with MTLS. Recurrent seizures were more common in both subgroups within 3 months post-surgery, and patients with MTLS had a more favorable prognosis than those with LTLE.

As previously mentioned, TLE is the most common type of drug-refractory epilepsy. According to the origin of the seizure, it can be divided into two subtypes, of which MTLS accounts for about two-thirds. Early diagnosis of MTLS is essential for a better prognosis. At present, patients with MTLS can be diagnosed based on electro-clinical symptoms and HS identified from MRI.[19,20] However, there is no unified standard in the diagnosis of MTLS and whether electro-clinical symptoms or HS is necessary for this diagnosis.[20] In this study, 27.8% of patients with MTLS did not have HS, thus implying that the HS is not a specific pathological mechanism in these patients.

Seizures are usually characterized by the abnormal EEG rhythm of the brain. It is essential to explore electrophysiological changes in patients with epilepsy. In the 1960s, the SEEG methodology was founded by Talairach and Bancaud. After the appearance of the stereotactic method, multiple electrodes were able to be implanted into different brain regions to record exact electrical activity. The observation of the relationship between the sequential activation of different brain regions and the manifestations of seizures may provide a theoretical basis for an epilepsy surgical plan.[21] In this study, there was a longer interval between the SEEG discharge and the presence of seizures in patients with MTLS. It indicated that other structures of the temporal lobe or other brain regions of the lateral temporal lobe may participate in the propagation of MTLS. Therefore, the standard anterior temporal lobectomy would be useful in these patients. In patients with LTLS, the abnormal SEEG discharge rapidly spread to other structures of the temple lobe, which could gradually contribute to the epileptogenic network. As a result, the standard anterior temporal lobectomy may not be suitable for these patients.

In summary, patients with MTLS account for about three-fifths of patients with TLE, and their long-term prognosis is more favorable than patients with LTLS. On the whole, a quarter of patients with TLE had no HS. Recurrence of seizures is more likely to occur within 3 months post-surgery.

There were some limitations in this study. A major limitation includes the small sample size and lack of contrastive analysis between scalp EEG and SEEG. Another limitation was the lack of relationship between seizure onset patterns and surgical outcomes.

In conclusion, patients with MTLS and LTLS had distinct SEEG ictal onset patterns, and patients with MTLS had a more favorable surgical outcome.

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Conflicts of interest

None.

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