



## The surgical outcome of patients with bilateral temporal lobe epilepsy

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### ABSTRACT

**Objectives:** The purpose of this study is to explore the surgical outcome of unilateral anterior temporal lobectomy (ATL) for patients with bilateral temporal lobe epilepsy (BTLE).

**Methods:** We retrospectively reviewed the data of patients who were diagnosed with BTLE by scalp electroencephalogram (EEG) and underwent ATL from 2001 to 2015. In addition, 80 patients were randomly selected as a control group.

**Results:** One hundred seventeen patients were included in this study and were divided into four groups by intracranial recordings as follows: 78 patients with unilateral seizure onset (Group 1), 13 patients with lateralizable dominant seizure onset (Group 2), 14 patients with lateralizable neuroimaging abnormalities (Group 3), and 12 patients without lateralizable dominant seizure onset or neuroimaging abnormalities (Group 4). The 12 patients in Group 4 declined surgical resection, whereas the remaining 105 patients received ATL, and 93 of them were followed up for more than 1 year after surgery. At the 1-, 2-, and 3-year follow-ups the percentage of patients who were seizure free was 52.9%, 56.5%, and 58.9%, respectively. For the mean postoperative efficacy, there was a statistical difference in patients who were seizure free either between Group 1 + Group 2 + Group 3 and the control group (44.1% vs. 67.5%,  $p = 0.002$ ), or between Group 1 and the control group (48.5% vs. 67.5%,  $p = 0.019$ ), or between Group 2 + Group 3 and the control group (32.0% vs. 67.5%,  $p = 0.002$ ). However, the difference was significant only at the first year follow-up, and there was no significant difference afterward.

**Significance:** Although the surgical outcome of patients with BTLE is not as good as that of patients with unilateral TLE in short-term follow-up, quite a portion of these patients could benefit from unilateral temporal lobe resection in the long term.

### 1. Introduction

Patients with temporal lobe epilepsy (TLE) are thought to be good candidates for epilepsy surgery. However, the proportion of patients who are seizure free following anterior temporal lobectomy (ATL) remains suboptimal, with a seizure-free rate at short-term follow-up between 66% and 70% (McIntosh et al., 2001; Spencer and Huh, 2008; Tellez-Zenteno et al., 2005; West et al., 2015). Patients with bilateral temporal lobe epilepsy (BTLE) are thought to be one of the reasons for the low rate of seizure freedom (Andrade-Machado and Benjumea-Cuartas, 2016; Barba et al., 2016). Although the traits and treatments of BTLE were discussed in some previous reports (Boling et al., 2009; Chkhenkeli et al., 2013; Ding et al., 2016; Kuba et al., 2003), the strategy of diagnosis and treatment of BTLE is still controversial. Some reports showed relatively good results of epilepsy surgery for patients

with BTLE (Aghakhani et al., 2014; Boling et al., 2009; Di Vito et al., 2016; Hirsch et al., 1991a; Sirven et al., 1997), but it is still commonly considered that surgical treatment should not be considered in patients with BTLE (Didato et al., 2015). Actually, the diagnostic criteria and surgical procedure in different reports were not the same. Therefore, more surgical data are needed to evaluate the surgical outcome under the same criteria and procedure.

In this article, we present the data of patients with BTLE according to the same criteria and who received the same process of surgical evaluation at a single epilepsy center. BTLE was diagnosed when the patient showed at least one of the following features according to long-term video electroencephalogram (EEG) monitoring: 1) the ictal EEG simultaneously involved the two temporal lobes, without the possibility of lateralizing its onset in at least one seizure; 2) the lateralizable features of semiology were inconsistent to the ictal EEG; and 3) the ictal

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EEG alternately arose from the two temporal lobes in at least two different seizures. Referring to Didato's definition (Didato et al., 2015), seizures with the traits of 1 and/or 2 were classified as non-lateralizable bitemporal seizure, and seizures with the trait of 3 were classified as independent bitemporal seizure. We discuss the treatment strategy and surgical outcome of BTLE according to these criteria.

## 2. Methods

### 2.1. Patient selection

We retrospectively reviewed the clinical data of patients who underwent surgical treatment for medically intractable epilepsy at the Comprehensive Epilepsy Center of Beijing between October 2001 and October 2015. Patients who met all these conditions were included: 1) Patients who were diagnosed with BTLE according with our criteria; 2) patients who received bilateral intracranial electrode implantation to lateralize the epileptogenic zone (EZ); and 3) patients who were identified as having TLE according to the intracranial recording.

In addition, a comparable number of patients during the same period were randomly selected as a control group. In these patients, the EZ could be localized by non-invasive investigation, and unilateral ATL was performed in these patients.

### 2.2. Presurgical evaluation

#### 2.2.1. Magnetic resonance imaging

All the patients underwent a high-resolution magnetic resonance imaging (MRI) protocol that was performed using a 1.5 T or 3.0 T MR Scanner (Siemens, Munich/Erlangen/Verio, Germany) and consisted of conventional spin-echo T1-weighted axial, sagittal, coronal, and T2-weighted axial sequences (section thickness of 5 mm, image gaps of 1 mm). In addition, fluid attenuated inversion recovery (FLAIR) images were obtained with a thickness of 5 mm. The transversal and coronal sections were respectively acquired in parallel with or perpendicular to the long axis of the hippocampal formation. Three-dimensional (3D) anatomical T1-weighted axial, sagittal, and coronal sequences covering the whole brain volume with a 1-mm section thickness also were performed to observe the cortical structure.

#### 2.2.2. Scalp video-EEG monitoring

Long-term scalp video-EEG monitoring was performed for each patient (Micromed, Treviso, Italy). The scalp electrodes were arranged according to the international 10–20 electrode system, and as a rule, sphenoidal electrodes were inserted. The duration of scalp video-EEG monitoring ranged from 3 to 14 days, and at least more than three habitual seizures were recorded to determine the seizure onset zone. The anti-epileptic drugs (AEDs) were usually reduced gradually to facilitate the recording of seizure. The seizure onset and the propagation characteristics were analyzed independently by two EEG experts who were aware of the clinical and neuroimaging data [e.g., MRI, positron emission tomography-computed tomography (PET-CT), and magnetoencephalogram].

#### 2.2.3. Principle of intracranial electrode placement

For the patients who were diagnosed with BTLE according to long-term video-EEG monitoring, bilateral subdural or depth electrodes were implanted according to the information acquired from non-invasive presurgical evaluations. Usually, the bilateral depth electrodes were placed stereotactically into hippocampal structures by a posterior lateral approach. The subdural strip electrodes were placed through burr holes to cover the temporal cortex, especially the basal temporal cortex, or the cortex surrounding the sylvian fissure, and even the frontal cortex. All the patients in control group did not undergo invasive EEG recording.

### 2.2.4. Intracranial EEG monitoring

Intracranial EEG (iEEG) monitoring was performed to further lateralize and localize the EZ. The iEEG sampling rate was set at 1024 Hz for recording more details of seizure propagation. At least more than three habitual seizures were recorded for each patient. The majority of seizure onset zones were identified visually on iEEG traces during the long-term iEEG monitoring. According to the seizure onset recorded by iEEG, the patients were further classified as patients with lateralizable bitemporal seizures and independent bitemporal seizures.

### 2.3. Classification and surgery

The surgical resections were planned according to the result of iEEG and other non-invasive results. Classical ATL was performed for patients (less than 4.5 cm in length in left temporal lobe and less than 5.5 cm in length in right temporal lobe, including mesial temporal structure and hippocampus). Additionally, intra-operative ECoG before and after the resection was performed. Supplementary tailored resections were performed for some patients with obvious residual epileptic activities in posterior temporal cortex.

The patients were classified into four groups. Group 1: the patients who demonstrated unilateral temporal seizure onset by iEEG and underwent ATL. Group 2: the patients whose iEEG demonstrated bilateral seizure onsets with dominant laterality (So et al., 1989) (> 80% of the seizures recorded from one temporal lobe) and underwent ATL of the dominant side. Group 3: the patients who demonstrated seizures originating from each temporal lobe independently without significant lateralized predominance, whereas unilateral specific neuroimaging abnormalities were found in one temporal lobe. These patients also received ATL in accordance with the abnormal MRI findings. Group 4: the remaining patients whose iEEG showed independent bilateral seizure onset and without seizure laterality or lateralizable MRI abnormalities. Instead of resective surgery, some of these patients received vagus nerve stimulation (VNS) or deep brain stimulation (DBS), and some patients elected to postpone the surgery and continue pharmacological treatment.

### 2.4. Follow-up and outcomes

After ATL, patients were followed up for at least 12 months to observe surgical outcomes. The postoperative AEDs were usually remained unchanged after operation if the AEDs were appropriate before operation. Occasionally, we postoperatively reduced the number of AEDs to two with reasonable dose for some patients who had more than two kinds of AEDs. Follow-up information was based on outpatient and hospital visits, questionnaires during visits, and telephone interviews. Long-term outcome classification (OC) proposed by the ILAE Commission Report was performed to report the patients' postoperative outcome (Wieser et al., 2001). The definition of each OC was as follows: OC1 means patient achieved complete freedom from seizure and without auras; OC2 means only auras and no other seizures; OC3 means patient had one to three seizure days per year that included auras. Patients with an outcome of OC1 to OC3 were seen as patients with good outcome.

### 2.5. Statistical analysis

Analysis of variance and Fisher's exact probability test were used to compare the age of seizure onset/surgery, disease duration, the mean postoperative follow-up, and gender composition among four groups. Mann-Whitney tests were used to compare the age at the time of onset, the age at the time of surgery, disease duration, and the mean time of follow-up between two groups. Kaplan-Meier survival analysis was applied to calculate the probability of seizure freedom in the overall group over time. All statistical data analyses were conducted using SPSS software (version 17.0, SPSS, Inc., Chicago, Ill., USA). A p-value < 0.05 was considered significant.

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