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Prognostic factors analysis of frontal lobe epilepsy surgery.

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Abstract

Frontal lobe epilepsy (FLE) surgery is the second most likely pharmacoresistant focal epilepsy benefitting from surgical treatment secondary to temporal lobe epilepsy (TLE). This study aims to investigate the clinical characteristics of frontal lobe epilepsy and analyze the factors associated with the prognosis of surgery. 27 patients confirmed with frontal lobe epilepsy by surgery from 2010 to 2014 were enrolled in this study. The clinical characteristics of frontal lobe epilepsy and the epileptogenic focus position were analyzed. Engel and International League Against Epilepsy (ILAE) classification were used for prognostic analysis. The prognosis of 17 (63%) patients reached Engel class I, and that of 15 (56%) patients reached ILAE class I. The prognosis of patients with epileptogenic focus resection was better than lesion disconnection and thermocoagulation, but no significant difference. The epileptogenic focus position and negative magnetic resonance imaging (MRI) were not the factors for surgical prognosis. The prognosis of frontal lobe epilepsy is overall good. The preoperative assessment of individual and complete resection of lesion is the key for surgical prognosis.

Keywords: Frontal lobe epilepsy, Epilepsy, Surgery, Prognosis.

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Introduction

The Frontal Lobe Epilepsy (FLE) accounts for 1/4 of the refractory epilepsy [1], and has good outcome of surgical treatment. About 50% patients with frontal lobe epilepsy can obtain Engel I or International League Against Epilepsy (ILAE) I grade surgical prognosis [2,3]. However, the surgical prognosis of frontal lobe epilepsy is poorer than medial temporal lobe epilepsy [4-8].

It is reported that, the negative magnetic resonance imaging (MRI) performance [9], generalized scalp Electroencephalography (EEG) abnormalities [10] and preoperative frequent episodes are the main factors affecting the surgical prognosis of frontal lobe epilepsy. The early diagnosis of frontal lobe epilepsy can lead to the short disease duration, and the lesion in non-functional area often indicates a good prognosis [11]. There are different surgical methods and standards for each epilepsy treatment center.

Analysis with single prognostic classification cannot reflect the value of individual treatment. The prognosis analysis of epilepsy patients is mostly focused on the amelioration of seizure degree, and ignores the drug treatment, intelligence and social living ability. The goal of our study is to examine seizure-freedom following frontal lobectomy and risk factors in a cohort of FLE patients who had undergone FLE surgery at Jinan Central Hospital Affiliated to Shandong University, China.

Materials and Methods

Clinical data

27 patients confirmed with frontal lobe epilepsy in Jinan Central Hospital Affiliated to Shandong University (Jinan, China) from 2010 to 2014 were enrolled in this study. Data collected included gender, age, age at seizure onset and at surgery, seizure semiology, dates of surgery, of seizure recurrence, and of last follow-up, side of surgery. There were 18 males and 9 females. The patient's age was 3-53 years, with mean age of 21.85 ± 10.83 years. The age of epilepsy onset was 0-32 years, with mean age of 9.39 ± 8.16 years. The epilepsy duration was 1-27 years (mean 12.52 ± 7.86 years). Only one patient has the family history of epilepsy (patient's farther). No females were pregnant during the study. The intracranial monitoring was performed in 7 cases. The postoperative follow-up was conducted for more than 12 months. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Shandong University. Written informed consent was obtained from all participants.

Preoperative patient evaluation protocol

After patient admission, the detailed disease history was inquired, and the nervous system examination was performed. The long-term video EEG monitoring with electrodes placed according to the International 10-20 system was conducted on all patients, using 128/64 long-term Video-EEG (VEEG) system (Nicolet Instrument. Inc., WI, USA). The craniocerebral MRI examination was performed using GE 1.5T superconductive MRI system (GE Healthcare, WI, USA), containing conventional axial, sagittal and coronal Tl-weighted volume acquisition, T2-weighted and Fluid-Attenuated Inversion Recovery (FLAIR) imaging. The neuropsychological assessment was performed on all patients. Part of patients underwent Positron Emission Tomography (PET) and/or intracranial EEG monitoring. Subdural electrodes and/or depth electrodes were implanted for any of the following reasons: (a) to confirm the ictal onset zone if scalp EEG information was either nonlocalizing or inconsistent with other noninvasive investigations such as MRI or seizure semiology; (b) to perform functional mapping preoperatively if the ictal onset zone was thought to be close to eloquent cortex; and (c) whenever a multifocal epileptogenic process was suspected based on multifocal noninvasive EEG findings or multilobar involvement on imaging.

Surgical method

All 27 patients received were surgical treatment. There were 20, 5 and 2 cases with epileptogenic focus resection, epileptogenic focus disconnection and epileptogenic focus resection combined with cortex thermocoagulation, respectively.

Prognosis assessment

The prognosis was assessed using Engel postoperative classification and classification of ILAE. Engel class I and Engel class II were defined as good prognosis, and Engel class III and Engel class IV were defined as poor prognosis. The ILAE classification system 1, 2 and 3 were defined as good prognosis, 4 and 5 were defined as poor prognosis.

Follow-up

After surgery, the patients took routine antiepileptic drugs. The follow-up was performed once every 3-6 months, and the regular EEG was conducted.

Statistical analysis

The statistical analysis was carried out using SPSS17.0 software (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± SD. Comparisons between two groups were performed using t test using one-factor analysis of variance. P<0.05 was considered as statistically significant.

Results

General data

67 epilepstic seizures were recorded in 27 patients, including 2 cases of aura, 4 cases of bilateral asymmetric tonic seizure, 9 cases of unilateral tonic, 3 cases of hypermotor, 5 cases of GTCS, 4 cases of autonomic symptom, 4 cases of versive seizure, and 2 cases of incontinence of urine. All 27 patients underwent surgical treatment and were followed up for 12-24 months. There were 19 (70%) cases have good outcome. The side of the lesion, age at onset, age at surgery, Leision location were not associated with surgical outcome (Table 1).

Table 1. *General data of patients.*

Index	Total (n)	Good prognosis	Poor prognosis
Sex (female/male)	10/17	7/12	3/5
Lesion side (L/R)	11/16	7/12	4/4
Onset age (0-32 years)	9.39 ± 8.16	8.63 ± 6.13	7.75 ± 5.08
Surgery age (3-53 years)	21.85 ± 10.83	22.38 ± 9.28	21.0 ± 6.33
Epilepsy duration (1-27 years)	12.52 ± 7.86	13.88 ± 6.38	13.25 ± 6.96

Table 2. *Engel classification of prognosis in 27 patients.*

Engel classification	Description	Before surgery (n)	After postoperative 1 year (n)
I	Seizure disappeared	17	13
II	Rare seizure, 2-3 times one year	2	2
III	Significant improvement; seizure was reduced by more than 90%	7	10
IV	No significant improvement; seizure was reduced by less than 90%)	1	2

Table 3. *ILAE classification of prognosis in 27 patients.*

ILAE classification	Description	After postoperative 1 year (n)
1	No seizure	15
2	Only presymptom attack	2
3	Seizure occurred 1-3 times one year	2
4	Seizure<50% of before surgery	5
5	Seizure between 50%-100% of before surgery	3
6	Seizure>100% of before surgery	0

Surgery outcome

No patient died after the surgery. The intracranial infection occurred in 1 patient, and subcutaneous effusion occurred in 2 patients. Assigned Engel outcome classes 17 (63%) patients had a class I outcome and 15 (56%) were assigned an ILAE class 1 outcome. which is different from an Engel class I outcome because it allows for auras. The postoperative ILAE and Engel classification were shown in Tables 2 and 3.

Relation between epileptogenic focus resection and prognosis

There were 20 patients with epileptogenic focus resection, including 14 (70%) cases of Engel class I. Five patients were treated by epileptogenic focus amputation, including 3 (60%) cases of Engel class grade I. Two patients were treated by epileptogenic focus resection combined with cortex thermocoagulation, among which 1 case was with Engel class I (50%). The prognosis of patients with epileptogenic focus resection was better than lesion disconnection and thermocoagulation, but no significant difference (Table 4).

Table 4. Relation between surgery mode and prognosis.

Surgery mode	Total (n)	Good prognosis (n)	Poor prognosis (n)
Epileptogenic focus resection	20	15	5
Epileptogenic focus disconnection	5	3	2
Epileptogenic focus resectionombined with cortex thermocoagulation	2	1	1

Relation between epileptogenic focus position and prognosis

Nine patients had epileptogenic focus on medial frontal lobe (including SMA zone), including 5 cases of Engel class I. Eleven patients were with epileptogenic focus on lateral frontal lobe, including 7 cases of Engel class I. Three patients were with epileptogenic focus at the frontal pole, including 2 cases of Engel class I. Four patients had epileptogenic focus on basil frontal lobe (including orbital frontal gyrus), including 3 cases of Engel class I (Table 5).

Table 5. Relation between epileptogenic focus position and prognosis.

Epileptogenic focus position	Total (n)	Good prognosis (n)	Poor prognosis (n)
Medial frontal lobe	9	6	3
Lateral frontal lobe	11	8	2
Frontal pole	7	5	2

Relationship between the clinical symptom and prognosis

67 seizures were recorded in this study. All auras and seizure were recorded by VEEG monitoring system for preoperative analysis. According to Dr Luders Semiological seizure classification, the following ictal semiology was considered lateralized or localized: contralateral somatosensory and visual auras; contralateral tonic, clonic seizures; contralateral nystagmoid eye deviation or versive seizures [12]. The lateralizing and/or localizing symptoms including unilateral tonic/clonic seizure and versive seizure are analyzed. There were 19 patients with lateralizing and/or localizing symptoms, among whom 13 (68%) cases had good prognosis, with poor prognosis in 6 cases (Table 6).

Table 6. Relation between clinical symptom and prognosis.

Clinical symptom	Total (n)	Good prognosis (n)	Poor prognosis (n)
Aura	2	1	1
Unilateral tonic/clonic	9	7	2
Eye deviation	4	3	1
Asymmetrical tonic	4	2	2

Relation between postoperative pathology and prognosis

The postoperative pathology confirmed 16 cases of Focal Cortical Dysplasia (FCD), 12 (75%) cases have a good outcome. Four cases of necrosis combined with glial hyperplasia scar merger, 3 cases of encephalitis, 2 cases of Dysembryoplastic Neuroepithelial Tumor (DNET), 1 case of vascular malformation, and 1 case of cysticercosis (Table 7).

Table 7. Relation between postoperative pathology and prognosis.

Epileptogenic focus position	Total (n)	Good prognosis (n)	Poor prognosis (n)
FCD	16	12	4
Others	11	7	4

Discussion

Epilepsy is a common seizure disorder of nervous system. The frontal lobe epilepsy is a more common type, accounting for 25% of epilepsy [1,13]. Its incidence is the second only to temporal lobe epilepsy [14]. The refractory epilepsy is often difficult to be controlled by Antiepileptic Drugs (AEDs). It requires surgical intervention, but the prognosis is poorer than temporal lobe epilepsy. In this study, there are 63% cases with postoperative Engel class I, while Engel class I and Engel class II account for 70% of total cases. This is similar to previous studies [3,15,16]. The detailed preoperative evaluation is the premise to improve the cure rate. The purpose of the surgical treatment is to stop the postoperative seizure and reduce the deletion of nerve function as little as possible. Frontal lobe contains primary motor area (M1), premotor area, language area (Broca's language area), frontal eye area, Supplementary Motor Area (SMA), orbitofrontal gyrus and negative motor area. The clinical manifestation of epileptic seizure is complex. The asymmetric tonic seizure, unilateral tonic/clonic seizure and hypermotor seizure are generally considered as the characteristics of frontal lobe epileptic seizure [17,18].

The epilepsy with lateralizing and/or localizing symptoms has good prognosis [19]. It is found that, the epilepsy in which the clinical electrical symptomatology conforms to imaging has good prognosis [6]. Results of this study show that, the patients with versive seizure and tonic/clonic seizure have good surgical prognosis. The complete resection of epileptogenic focus is the key of surgical success. Due to the complexity of frontal function area, when the lesion closes or locates in the function area, the risk of function deficit after surgery is large. Therefore, the detailed preoperative evaluation and accurate brain function location are needed, especially for cases in which the frontal lobe medial surface EEG and clinical symptoms lacking lateralizing and/or localizing value [20]. When necessary, the intracranial electrode monitoring and brain function mapping are applied. In this study, 7 patients were applied with the intracranial subdural electrodes, among whom 1 case with epileptogenic focus in M1 area only received cortex thermocoagulation treatment. The postoperative follow-up found that they were with Engel class III. The cure rate in epileptogenic focus total resection group was higher than the epileptogenic focus amputation group.

FCD, tumor, scar after traumatic brain injury and encephalitis can cause epileptic seizure. According to the literature [21], focal cortical dysplasia type I is related to temporal lobe seizures [14,19]. In patients with FCD type II, multilobar lesions are found, involving hemisphere, often with extratemporal location and mainly in the frontal lobe. Epileptic seizures in focal cortical dysplasia are difficult to control with pharmacological treatment and often intractable. 60-80% of patients remain seizure-free after surgery, depending on the study center [22,23]. Our study shows no different of surgery outcome between FCD and other lesions. The FCD type I is MRI negative, which is one of the reasons of the underlying frontal lobe epilepsy. The type II FCD has the clear imaging changes in MRI, but the actual boundary is often wider than MRI performance. So the larger resection is needed in surgery to achieve a good outcome. The electrocorticography (EcoG) or intracranial subdural electrode were needed among these cases. Unfortunately, according to different authors, subtotal resection is seen in approximately 30% of patients [23]. If the lesion locates in the eloquent cortex, the intracranial electrode is required to stimulate the cerebral cortex, for function brain mapping [24]. There is no significant difference of prognosis between two types of surgery [25]. The intraoperative application of ECoG monitoring can obtain the complete resection of FCD.

Surgery is a valuable option for patients with frontal lobe epilepsy. In our study, presurgical tests were not found to have a significant predictive value for seizure freedom, it’s mean the presurgical evaluation of frontal epilepsy was complex. The preoperative assessment of individual and complete resection of lesion is the key for surgical prognosis. More patients and Multivariate analysis may helpful in study of the outcome of epilepsy.

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