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MRI NEGATIVE OR POSITIVE IS THE MAIN INFLUENCING FACTOR OF STEREOTACTIC RADIOFREQUENCY THERMOCOAGULATION OF AMYGADALAHIPPOCAMPL FOR THE TREATMENT OF MEDIAL TEMPORAL LOBE EPILEPSY

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ABSTRACT

Purpose To explore the influencing factor of therapeutic efficacy of depth electrode guided stereotactic radiofrequency thermocoagulation (RFTC) of amygadalahippocampl for the treatment of intractable medial temporal lobe epilepsy (MTLE). Methods One hundred and twenty seven cases of MTLE were retrospectively studied after depth electrode guided RFTC of amygadalahippocampl. MRI scan was performed to all patients with T1/T2/Flair sequence preoperatively, in which 60 cases were negative and 67 positive.Results With 24-83 months follow-up, 70(54.69%) patients were in Engel's class I–III in which 41(32.28%) in Engel I. Among them, 30/60 (50.00%) patients got seizure free in MRI-negative group, but only 11/ 67 (16.42%) cases in MRI-positive group got seizure free., Significant difference (P<0.001) was obtained between this two groups. Conclusion The outcome of seizure control after RFTC of amygadalahippocampl in preoperative MRI-negative patients was better than that in positive patients. MRI-positive MTLE patients must be carefully selected for RFTC of amygadalahippocampl.

Key Words: Medial temporal lobe epilepsy, Radiofrequency thermocoagulation, Amygadalahippocampl, MRI-negative.

INTRODUCTION

Although temporal lobectomy is the main approach for the treatment of temporal lobe epilepsy (TLE), stereotactic radiofrequency thermocoagulation (RFTC) of amygadalahippocampl is easy to be accepted by patients because of less invasive, especially for the treatment of medial temporal lobe epilepsy (MTLE). The epileptogenic zone located in medial temporal lobe (amygdala, hippocampus and parahippocampal gyrus) is more than 90% of the patients with TLE [1]. It's the substantial rationale for stereotactic coagulations of amygdalohippocampals to treat MTLE.

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Thermocoagulation of epileptic foci in medial temporal lobe is not a new technique as reported from 1950s to 1970s [2]. However, as lack of advanced techniques and equipments, some severe complications of coagulation were occurred especially in the coagulation of bilateral hippocampus [3]. The stereotactic coagulation for temporal lobe epilepsy was rarely reported in the last two decades of 20th century. With the development of MRI and depth electrode, stereotactic epilepsy surgery became resurgence all over the world. In Canada [4,5], France [6] and particularly by the group in Czech [7,8], it has been used to treat MTLE patients with unilateral epileptic foci in recent years.

However, most of them were emphasized in the technique of coagulation. The number of cases in each reported series was not more than one hundred.

No one noticed what kind of patients are more suitable for RFTC OF of amygadalahippocampl. To explore the influencing factor, we retrospectively studied 127 cases of MTLE who experienced RFTC of amygadalahippocampl include 10 cases of bilateral coagulation. According to preoperative MRI scan, we compared the results of seizure control between MRI-positive and MRI-negative patients and found it has a significant difference between these two groups.

METHODS

Patient selection

Since 2006, hundreds cases of MTLE patients were treated with depth-electrode-guided RFTC of amygadalahippocampl in Neurosurgery Department of Navy General Hospital of PLA in Beijing, China. All patients were advised to continue taking anti epileptic drugs (AEDs) without reducing dose at least 2 years after operation. The patients including in this study should meet the following standard: (1) fully match the criteria of MTLE, (2) intact preoperative MRI scan, (3) at least 2 year clinical follow-up, (4) precise postoperative evaluation of seizure outcome with Engel's classification. One hundred and twenty seven patients were included in this series.

Clinical material

Ninety one male and 36 female patients at the main age of 24.33±11.18 (range: 4 to 73) years old were included. The main duration of illness was 20.01±13.52 (range: 3 to 33) years. There were 29 patients with definite cause such as trauma, fever, hypoxia and encephalitis. The other 98 patients were no reason for the illness. All patients were diagnosed as MTLE, in which 92 were confirmed to be unilateral with long term video EEG (VEEG) combined with semeiology, the other 35 with invasive stereo EEG (SEEG) monitoring turned out to be unilateral in 25 and bilateral in 10.

Under the agreement of Ethics Committee of our hospital, they all signed the Informed Consent From for the operation and then experienced RFTC OF of amygadalahippocampl.

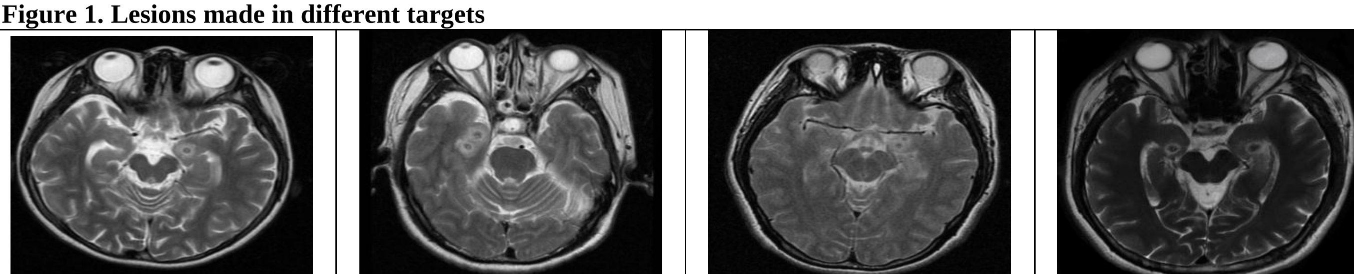
Preoperative MRI

MRI scans were performed to all patients with T1/T2/Flair sequence preoperatively. Sixty patients were negative and 67 positive. Among the MRI positive patients, there were 7 of encephalatrophy, 8 of hippocampus sclerosis, 8 of temporal lobe lesions, 8 of encephalomalacia, 19 of cortical dysplasia and 17 of others.

Surgical procedure

All of these patients refused to be treated with resection surgery. Under the agreement of Ethics Committee of our hospital, they all signed the Informed Consent From for the micro invasive operation and experienced depth electrode guided RFTC of amygadalahippocampl. The stereotactic procedure was the same as other reports. The fist target point was placed in the center of amygdala and the coagulations (70℃-75℃, 60s-120s, with interval of 2mm-3mm) were tailored by the recording of depth electrode. If the epileptic discharges did not decreased significantly after the first target coagulations, the lesion of next target 10 mm posterior to the former should be made subsequently. There were maximum 3 targets for coagulations in one side. Once bilateral independent epileptogenic zone was confirmed with preoperative SEEG, bilateral RFTC of amygadalahippocampl could be made during the same procedure. Unilateral coagulations were made in 115 cases, in which one-target lesion (figure 1a) was made in 85 cases, two-target (figure 1b) in 27 and three-target (figure 1c) in 5. Bilateral lesions (figure 1d)) were made in 10 patients.

Figure 1. Lesions made in different targets



A: one-target;	**B:** two-target;	**C:** three-target;	**D:** bilateral target

Evaluation of seizure control

Outcomes of seizure control were classified with Engel's classification [9] as showed in table 1. Class I was assessed as seizure free, class I+II as significantly effective and class I+Ⅱ+Ⅲ as effective.

Statistical analysis

Statistical analyses were performed with the IBM SPSS 20.0. Data are expressed as mean±SD. In order to access the difference of seizure control outcomes between MRI-negative and MRI-positive patients, Chi-square Significance Test (χ^2 Test)

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was applied to compare the constituent ratios of Engel's classification in different group. Quantitative parameters was analyzed with Non Paired-Samples T Test.

RESULTS

General outcomes of seizure control

With 24-83 months follow-up, 41 patients were in Engel's class I (Ia in 2, Ib in 15, Ic in 19, Id in 5) , while 7 patients in Engel's class II (IIa in 2, IIb in 5), 22 in Engel's class III (IIIa in 20, IIIb in 2) and 57 in Engel's class IV (IVa in 46 IVb in 9, IVc in 2). The seizure free rate was 32.28%, while significant effective rate rate was 37.80% and effective rate was 54.69%. There was no significant difference of seizure free rate related to the number of target (include bilateral-target) being coagulated as showed in table 1.

Table 1. Relationship between the number of target and seizure free outcome.

Group of target	free	non-free	Seizure free rate
One-target	26	59	30.59%
Two-target	10	17	37.04%
Three-target	2	3	40.00%
Bilateral-target	3	7	30.00%
χ^2			0.551
P			0.908

(Crosstabs Chi-Square Tests)

Deferent results between MRI-negative and MRI-positive patients

According to the preoperative MRI examination, we divided theses patients into two groups, MRI-negative and MRI-positive. The clinical features of these two groups were showed in table 2 and no significant difference was found on sex, age and duration of illness.

Table 2. Clinical features of MRI-negative and MRI-positive group

	negative	positive	χ^2 or *t*	*P*
Sex (male/female)	45/15	46/21	χ^2 =0.627	0.428
Age	24.33±11.18	20.01±13.52	*t*=1.949	0.053
Duration of illness	12.22±9.00	10.34±9.05	*t*=1.172	0.243

(Crosstabs Chi-Square Tests, Independent-Samples T test)

In 60 cases with negative preoperative MRI, 30(50.00%) patients got seizure free (Engle I). However, in 67 cases with positive preoperative MRI, only 11 (16.42%) patients became seizure free. Significant difference (P=0.000) was obtained between this two groups. See table 3.

Table 3. The results of seizure control between MRI-negative and MRI-positive group

Rate	MRI-negative	MRI-positive	χ^2	*P*
Seizure free	30/60（50%）	11/67（16%）	16.75	P<0.001
Significant effective	33/60（55%）	15/67（22%）	14.32	P<0.001
Effective	41/60（68%）	29/67（43%）	8.03	P=0.005

(Crosstabs Chi-Square Tests)

The subdivision of MRI-positive group according to the different structural lesions on MRI and there outcomes of seizure control are showed in table 4. There are no significant differences by Crosstabs Chi-Square Tests, but we noticed that the seizure free rates in subgroups of Encephalatrophy (3/7) and Hippocampus sclerosis (3/8) are relatively higher.

Table 4. MRI lesions and related postoperative outcomes

	Engel Ⅰ	Engel Ⅱ	Engel Ⅲ	Engel Ⅳ
Encephalatrophy	3/7	0/7	1/7	3/7
Hippocampus sclerosis	3/8	1/8	2/8	2/8
Temporal lobe Encephalomalacia	1/8	2/8	2/8	3/8
Extra temporal Encephalomalacia	1/8	0/8	3/8	4/8

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Whole cortical dysplasia	2/19	0/19	3/19	14/19
Others	1/17	1/17	3/17	12/17
χ^2	*8.192*	*7.927*	*2.091*	*8.737*
P	*0.146*	*0.160*	*0.836*	*0.120*

(Crosstabs Chi-Square Tests)

DISCUSSION

RFTC of amygadalahippocampl could be used as the first step for treatment of MTLE because of minimal invasive,.

Since MTLE is AEDs resistance, resection surgeries are widely used such as Anterior Temporal Lobectomy and Selective Amygdalohippocampectomy. However, being afraid of open cranial surgery, especially for the complications such as hemiplegia, hemianopsia, amnesia and so on, many patients would like to choose micro invasive procedure such as RFTC of amygadalahippocampl. To improve the outcome of seizure control for RFTC of amygadalahippocampl, a lot of modifications had been made in recent years. Catenoix H, et al connected a radiofrequency lesion generator system to SEEG electrode for coagulation during operation. Among 41 patients, 20 cases (48.7%) experienced a seizure frequency decrease of at least 50%, which was over 80% in 8 of them. One patient was seizure free [10]. Liscak R, et al, used a string electrode with a flexible 10-mm active tip to make the coagulations in a relative larger area by rotating 45 degrees in turn. Thirty-two patients were followed up over at least 2 years, and 25 of them (78%) were Engel I [11]. Daniel J. Curry, et al, reported MR-guided stereotactic laser ablation of epileptogenic foci, in which allows for real-time thermal monitoring of the ablation process and feedback control over the laser energy delivery. All 5 patients are seizure free and there were no complications as of 2–13 month follow-up [12]. In our series of 127 patients, we made lesions under guiding of depth electrode recording, 41 patients were seizure free. It means 32.28% of MTLE patients could be avoid for resection surgery. Furthermore, in MRI-negative patients, the seizure free rate was 50% (30/60). Thus, although resection procedure is more effective, since RFTC of amygadalahippocampl is characterized by minimal invasive, it is worth to be the first step for the treatment of MTLE, especially for MRI-negative patients.

MRI-negative patient is more suitable for RFTC of amygadalahippocampl

Originally, we thought that more coagulation would lead to a better result of seizure control. However, as showed in Table 1, there was no significant difference of seizure control to the number of target (include bilateral-target) being coagulated. This result is quite near the report by Malikova H, et al, that is: *different volume reduction, similar clinical seizure control* [13]. Nevertheless, when we divided our subjects to MRI-negative and MRI-positive groups, the ages and illness durations were compared with SPSS 20.0, no significant difference was found between these two groups as showed in Table 2, but the outcomes of seizure control were much better in MRI-negative patients. As showed in Table 3, there were 30/60 (50%) cases obtained seizure free (Engel I) after RFTC of amygadalahippocampl with preoperative negative MRI, but only 11/67 (16%) in MRI-positive patients. This result is quite different from that of resection surgery. We suppose the reason is, for MRI-negative patients, epileptic discharge is only the cause of seizure attack, in which could be resolved during RFTC of amygadalahippocampl under the guiding of depth electrode recording. On the contrary, for MRI-positive patients, although electrophysiologic examination indicates that epilepic discharges were mostly concentrated in medial part of temporal lobe, the lesions showed on MRI might be still responsible for seizures, in which couldn't be coagulated entirely even for hippocampal sclerosis. Therefore, it should be very careful to choose MRI-positive patients for RFTC of amygadalahippocampl

MRI-positive patients should be treated with resection surgery

Recent years, MRI plays a major role for not only localizing epileptic focus but also predicting postoperative outcomes. In epilepsy surgery, although electrophysiologic examination, especially SEEG has been supposed to be the golden standard for localization of epileptogenic zone, but we couldn't put depth electrodes to everywhere of whole brain, even SEEG can't provide us the entire electro physiologic features of epileptic patients. Better results after resection surgery would be obtained in MRI-positive patients [14]. In MRI-negative patients, the outcomes of postoperative seizure control were poor unless the epileptic focuses could be confirmed by PET [15]. According to economic reason, PET was not used in our 60 MRI-negative patients, so we didn't know if they were suitable for resection surgery, at least, they were not the best candidates of resection surgery. Conversely, some of those 67 MRI-positive patients, such as 8 cases of hippocampus sclerosis and another 8 cases of temporal lobe encephalomalacia, should be treated with temporal lobectomy. As they all refused to resection procedure, RFTC of amygadalahippocampl was the acceptable approach for them. Under the agreement of Ethics Committee of our hospital, they all signed the Informed Consent From for the operation and then experienced RFTC OF of amygadalahippocampl. As showed in Table 4, the outcomes of seizure control were with significant difference between MRI-negative and MRI-positive groups. The results of MRI-positive group were not satisfied after RFTC. Thus, MRI-positive patients should be treated with resection surgery which could remove either epileptic discharges or correlated structural lesions..

The outcomes of RFTC of amygadalahippocampl are different in subgroups of MRI-positive patients according to the characteristic of structural lesions

Despite no significant difference between MRI lesions and correlated outcomes of seizure control, we can still find some trend in Tab 4, that is, the encephalatrophy on MRI and hippocampal sclerosis is relatively better. According to Felix Rosenow & Hans Luders, there are five zones correlated to seizure attack, such as the symptomatogenic zone, the irritative zone, the seizure onset zone, epileptogenic lesion and the epileptogenic zone [16]. In our series, encephalatrophy on MRI might not be related to seizures, 3 (42.86%) in 7 cases got seizure free after RFTC of amygadalahippocampl. Hippocampal sclerosis is certainly the real epileptogenic lesion, 3 (37.5%) in 8 cases obtained seizures free. As we couldn't coagulate the whole sclerous hippocampus, the seizure free rate was still lower than that of MRI-negative patients. If the string electrode with a flexible 10-mm active tip mentioned by Liscak R, et al [11] was used to coagulate the whole hippocampal sclerosis, the more patient would get seizure free after RFTC of amygadalahippocampl. However, we couldn't use this technique in bilateral MTLE because of the larger damage of bilateral hippocampus would affect memory function of the patients [3]. Conversely, no matter encephalomalacia located in temporal lobe or extra, it might be still the epileptogenic lesion even though electrophysiologic examination indicates that epilepic dischaarges were mostly concentrated in medial part of temporal lobe. As temporal lobe lesion is near the site of coagulation, the effective cases (Engel I+II+III) was 5 (62.5%) in 8, although only 1 (12.5%) got seizure free because we couldn't deal with the lesion directly. Extra temporal lobe lesion is far from the coagulation site, we can only break down the pathway of epileptic discharges, the effective cases were 4 (50%) in 8, little bit worse than that of temporal lobe lesion. Most whole cortical dysplasia were caused by encephalitis and hypoxic-ischemic encephalopathy which was certainly the main cause of epilepsy [17], but we couldn't coagulated the whole cortex, so the results were quite poor, 14 (73.68) in 19 cases were in Engel IV. Consequently, although the outcome of seizure control is better in MRI-negative cases, MTLE patients with hippocampal sclerosis or other lesions without any relationship of seizures might be still the candidates for RFTC of amygadalahippocampl . However, since cases in MRI-positive patients were not enough for statistic analysis with *p* values to the outcomes of seizure control among subdivided groups. Further studies with accumulation of cases are needed so as to make a correct evaluation.

CONCLUSION

Preoperative MRI negative or positive is the main influencing factor of the outcome of seizure control after RFTC of amygadalahippocampl in MTLE patients. The outcome of seizure control is better in MRI-negative patients. In MRI-positive cases, it should be carefully used in choosing candidates since RFTC of amygadalahippocampl can not deal with the structural lesions thoroughly. Hippocampal sclerosis or other seizure relevant structural lesions on MRI might be got better result after improvement of the technique which could coagulate the whole structural lesions. Nevertheless, further studies with accumulation of cases are needed in order to make a scientific judgment.

ETHICS AND CONSENT

All human studies have been approved by the appropriate ethics committee and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Patients' parental guardians gave their informed consent prior to their inclusion in this study.

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DISCLOSURE

We confirm that none of the authors has any conflict of interest to disclosure. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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