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Clinical outcomes after medial temporal lobe epilepsy surgery: Anterior temporal lobectomy versus selective amygdalohippocampectomy

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ABSTRACT

Objective: To compare the anterior temporal lobectomy (ATL) with transsylvian selective amygdalohippocampectomy (SeAH) in 72 patients with medial temporal lobe epilepsy (MTLE) regarding the seizure control and neuropsychological outcomes.

Methods: Clinical data and follow-up data were collected and retrospectively analyzed. SeAH and ATL were used in 39 and 33 patients, respectively. All eligible patients were followed up at least one year. Wechsler Adult Intelligence Scale-Revised and the Wechsler Memory Scale-Revised were used to test the patients' neuropsychology before and after the surgery for one year.

Results: Fifty-nine patients (81.9%) achieved satisfactory seizure control (62.5% Engel Class I and 19.4% Class II). ATL obtained 84.8% satisfactory seizure control (28 patients), and the success rate was 79.5% (31 patients) for SeAH. There was no significant difference in seizure control between SeAH and ATL ($P=0.760$). The postoperative verbal IQ of SeAH group increased significantly in both side surgery ($P<0.05$), while the increase was not significant in the group of ATL of both side surgery ($P>0.05$). Regarding left-side surgery, postoperative verbal memory and total memory were increased significantly in the group of SeAH ($P<0.05$), while the increases were not significant in the group of ATL ($P>0.05$). In the right-side surgery, postoperative verbal memory and total memory were increased significantly in the two surgery strategy groups ($P<0.05$), while no significant increases were seen in non-verbal memory of the two surgery strategy groups ($P>0.05$).

Conclusion: Microsurgery for the treatment of refractory MTLE is successful and safe, and should be encouraged. The seizure outcome is not different between ATL and SeAH, while regarding as verbal IQ and verbal memory outcomes, SeAH may be superior to ATL in dominant hemisphere surgery.

KEY WORDS

medial temporal lobe epilepsy; anterior temporal lobectomy; selective amygdalohippocampectomy; seizure control; neuropsychology

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颞叶内侧癫痫手术治疗：前颞叶切除术与选择性杏仁核海马切除术

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[摘要] 目的: 比较前颞叶切除术(anterior temporal lobectomy, ATL)与经侧裂选择性杏仁核海马切除术(selective amygdalohippocampectomy, SeAH)治疗颞叶内侧癫痫(medial temporal lobe epilepsy, MTLE)在控制癫痫发作和改善神经心理学结果方面的疗效。方法: 回顾性分析SeAH(39例)和ATL(33例)治疗的72例MTLE患者的临床资料和随访资料。临床心理评估采用Wechsler成人智力量表和Wechsler记忆量表。结果: 72例患者中59例(81.9%)获得满意的癫痫控制(62.5% Class I和19.4% Class II)。ATL组癫痫控制满意28例(84.8%), SeAH组满意31例(79.5%), 两者之间差异无统计学意义($P=0.76$)。SeAH组左侧和右侧手术后语言IQ评分均明显增加($P<0.05$), 而ATL组左侧和右侧手术后语言IQ评分增加无统计学意义($P>0.05$); 左侧SeAH手术后语言记忆和总记忆评分显著增加($P<0.05$), 但是左侧ATL手术后语言记忆、非语言记忆、总记忆评分增加无统计学意义($P>0.05$); 右侧手术两种术式的手术后语言记忆和总记忆评分显著增加, 非语言记忆评分增加无统计意义($P>0.05$)。结论: ATL与SeAH是治疗MTLE的有效安全的方法, ATL与SeAH两种术式对癫痫控制无明显差异, 但对术后语言智商和语言记忆而言, 在优势半球侧手术时SeAH优于ATL。

[关键词] 颞叶内侧癫痫; 前颞叶切除术; 选择性杏仁核海马切除术; 癫痫控制; 神经心理

Surgical treatment of intractable medial temporal lobe epilepsy (MTLE) is considered as an efficient and safe method^[1-3]. A Meta-analysis reported a significantly improved seizure control in 60%–70% of the surgically treated patients^[4] and the outcomes have improved in recent years. Anterior temporal lobectomy (ATL) used to be the most widely performed standard resection for treatment of MTLE, while the approach is associated with a risk of neuropsychological function deficits, especially memory impairment. Limited resection such as selective amygdalohippocampectomy (SeAH) is an operative procedure originally developed to remove the epileptogenic focus while reserve unaffected brain tissue from surgery and minimize the side-effect after temporal lobe surgery^[5-6].

There is still no consensus concerning the surgical approach and the extent of the resection to receive the most optimal surgical outcome: seizure freedom and good quality of life without additional neuropsychological impairment. It is widely accepted that there was no significantly difference between the two strategies regarding to seizure control except in condition that the temporal cortex involved the epileptogenic region. But there is still a debate on the side-effect especially on memory outcomes^[7-9]. Although it was difficulty to perform completely random control studies, some author has discussed. In 1982, Wieser et al^[5-6] introduced transsylvian SeAH approach and reported on a rather

small number of patients and found that SeAH produces less cognitive impairment than ALT. Some authors^[10-11] also confirmed that SeAH show better neuropsychological outcomes than ATL, at least in some part of memory. Some centers use this modality as the dominant approach. However, their findings were disputed when other studies produced different results. SeAH, like ATL, can cause cognitive decline. Some authors^[9, 12] showed there was no evidence proven the SeAH was better than ATL even on the dominant-side surgery. Therefore, neither SeAH nor ATL can be recommended over the other as a standard approach. It was an ongoing discussion topic for approach choice.

In the present study, the authors reported a consecutive series of patients who underwent either anterior temporal lobectomy (ATL) or transsylvian SeAH. This study was initiated to describe the clinical outcomes of the microsurgery outcomes of MTLE and analyze the effects of clinical factors, resection strategies, and histopathological findings on seizure outcomes. We also compared the two approaches regarding the postoperative neuropsychological performance to give another evidence for approaches choice.

I Patients and methods

I.1 Patients

A total of 72 patients (41 male, 31 female, mean age

23.5 years, ranged from 7 to 60 years) with MTLE were microsurgical treated (33 ATL or 39 SeAH) between 2004 and 2011 at the Department of Neurosurgery, Xiangya Hospital of Central South University by the senior neurosurgeon. Minimal requirements for inclusion in this study were as follows: Complete clinical, MRI, and electrophysiological data sets; at least 12 months follow-up. Five patients were excluded because of failure for follow-up. Clinical characteristics are presented in Table 1. The patients harboring tumors evaluated by MRI may underwent operation just after diagnosis, while the patients of non-neoplasm had undergone adequate trials of at least two first-line antiepileptic drugs before they were referred for preoperative evaluation.

Table 1 Clinical characteristics of patient with medial temple lobe epilepsy (n=72)

Characteristics	ATL(n=33)	SeAH(n=39)
Gender (male/female)	20/13	21/18
Age at surgery (range)/year	23.5(7–55)	23.6(10–60)
Age at onset/year	15.7	15.7
Duration of seizure/year	7.8	7.9
Side(left/right)	18/15	17/22
Major seizure type		
Auras	9	11
Simple partial seizures	5	5
Complex partial seizures	9	10
Generalized seizures	10	13
MRI examination		
Lesional changes	19	21
Hippocampal sclerosis	11	14
None	3	4

1.2 Preoperative evaluation

All patients underwent continuous, noninvasive, scalp, video-electroencephalogram (vEEG) monitoring. The EEG data were classified according to the location of interictal epileptiform EEG activity and ictal onset.

All patients underwent preoperative MRI assessments. T1-weighted, T2-weighted, and fluid-attenuated inversion recovery scans were routinely performed. Whenever a lesion or tumor was suspected, contrast-enhanced MRI was performed, while others of non-lesions, single-photon emission computed tomography (SPECT) was performed to evaluate the

blood perfusion of medial temporal lobe.

Neuropsychological examinations were performed preoperatively and at 12 months after surgery using Wechsler Adult Intelligence Scale-Revised (WAIS-R) and Wechsler Memory Scale-Revised (WMS-R). These examinations were performed in 2 sessions over 2 consecutive days. All tests were performed by one psychologist.

1.3 Surgical consideration and procedures

At the early stage of our study, we mainly used the ATL and from 2007, we used transsylvian approach mainly except for the lesion or the epileptogenic focus was expanded to the temporal neocortex, in which condition the ATL was used.

Standard anterior temporal lobectomy (sALT) was used in 33 patients. For sALT, the extent of resection limited to 4.0–5.0 cm from the temporal pole in the nondominant hemisphere and 3.5–4.0 cm in the dominant hemisphere, including the superior temporal gyrus. For some patients with neoplasma lesions and with limited intraoperative electrophysiological evoking monitoring underwent some smaller resections. Most of temporal and basal lesions were treated with an additional removal of the hippocampus and amygdala.

Transsylvian SeAH, introduced by Yasargil et al^[5-6], was used in 39 patients. After microsurgical dissection and anterior opening of the sylvian fissure, the temporal horn of the lateral ventricle was opened with a 15-mm incision of the temporal stem. First the caput hippocampi and amygdala were resected and the uncus was removed. Second, we performed en bloc removal of the corpus hippocampi together with the parahippocampal gyrus, preserving the arachnoid layers covering the cisterna ambiens. The lateral resection border was the sulcus collateralis, and the posterior resection should reach the middle brainstem level.

1.4 Follow-up and seizure control

All patients were called for follow-up regularly. Seizure control, blood anti-epileptics concentration, neuropsychological performance and visual field test were measured. According to Engel curative effect classification, seizure outcome was divided into 4 classes on the basis of the patients' last postoperative seizure status. For additional analyses, Class I and II outcomes were usually

summarized as a good or satisfactory seizure control, whereas Classes III and IV were listed as an unsatisfactory seizure control.

1.5 Statistical analysis

Chi-squared test was used to determine the correlation of seizure outcomes with the surgery strategies and other factors. For multifactorial analyses, forward stepwise logistic regression was performed with critical *P* levels of 0.1 for inclusion and 0.3 for exclusion of factors in the model, using adjusted χ^2 statistics. The result was confirmed with a backward stepwise regression. For full-scale IQ, verbal IQ and performance IQ of the WAIS-R, global, verbal and visual memory quotients (MQ) of WMS-R in the pre- and postoperative sessions, changes at group level were assessed using paired *t*-tests, and changes that between groups were assessed using ANOVA test. All reported *P* values were two-sided, and a value of *P*<0.05 was considered statistically significant.

2 Results

2.1 Neuroimaging findings

Structural abnormalities were detected in 65 patients (90.3%) and no abnormalities were detected on MRI in the remaining 7 patients. The most common finding was unilateral mesial temporal sclerosis with or without neoplasias-lesions. There were 40 patients demonstrated neoplastic lesions or cavernous hemangioma changes evaluated by MRI.

2.2 Histopathological findings

A standard neuropathological protocol was generally used for all epilepsy surgery cases. Tumors were classified according to the revised World Health Organization (WHO) Classification Scheme for Tumors of the Nervous System. Thirty-two lesions were non-neoplastic, most of which were hippocampus sclerosis. Other fourteen non-neoplastic findings were noted, including 4 cortical dysplasias, 7 cavernous hemangiomas, and 3 scars after brain injury. There were 3 patients with 2 pathological conditions, hippocampus sclerosis with cavernous hemangioma. Thirty-five lesions were neoplastic. All neoplasias were gliomas (9 tumors were WHO Grade I, 20 were WHO Grade II, and 6 were WHO Grade III).

2.3 Seizure outcomes

The mean follow-up period was 46 months (ranged from 14 to 108 months). A total of 45 patients (62.5%) were classified as seizure-free (Class I), and 14 patients (19.4%) experienced only rare seizures (Class II); these classes were grouped together as representing satisfactory seizure control (59 patients, 81.9%). Nine patients (12.5%) demonstrated improvements in seizure frequency of more than 75% (Class III), and no worthwhile improvement was observed in 4 patients (5.6%); these classes were grouped together as representing unsatisfactory seizure control (13 patients, 18.1%).

Thirty-eight patients (90.5%) with neoplasias pathology or cavernous angioma had satisfactory seizure control whereas 21 patients (70.0%) with non-neoplasias pathology had satisfactory seizure control. There was statistically significant difference (*P*=0.033) showed by univariate analysis. Thirty-three patients (89.2%) at right-side and 26 patients (74.3%) at left-side had satisfactory seizure control. There was no statistically significant difference (*P*=0.131). There was also no statistical difference in likelihood of seizure control between patients who underwent ATL and SeAH (*P*=0.760), and the satisfactory rate was 84.8% and 79.5%, respectively. The details are shown in Table 2.

Stepwise linear regression analysis confirmed independent effects of the lesional pathology (*P*=0.017), whereas the factor sex (*P*=0.269), side (*P*=0.150), duration of history (*P*=0.430), type of seizure (*P*=0.541) and all other tested items were excluded.

2.4 Complications

There was no operative mortality. Epidural hematoma occurred in 2 patients, 1 recovered by expectant treatment and the other needed an additional operation to remove the hematoma. Meningitis occurred in 1 patient. One patient experienced hemiparesis postoperatively due to vascular spasm of posterior communication artery, and recovered nearly to normal at the follow-up.

No patients complained visual field deficit, while, when tested by computed perimetric exam, 24 patients had visual field deficit and the rate was 33.3%. For visual field deficit, all of the patients were unilateral and most of the patients limited in one quarter of visual field. There was no statistically significant difference of visual field deficit between the ATL and SeAH (39.4% and 28.2%

respectively, $P=0.098$). No patients experienced visual acuity deterioration.

2.5 Neuropsychological outcomes

Preoperative and 1-year follow-up IQ outcomes are shown in Table 3. There were no patients experienced IQ and memory severely deterioration after surgery. The multivariate ANOVAs with type of surgery and the side of surgery as intergroup factors revealed that there were no significant preoperative group differences with respect to full-scale IQ, verbal IQ and performance IQ ($P>0.05$). The verbal IQ in the SeAH group of both side increased significantly ($P<0.05$), while in the group of ATL of both side, the increase was not significantly ($P>0.05$). The performance IQ was increased in all group but not statistically significant ($P>0.05$). The significant increase of the full-scale IQ was only seen in left-side SeAH group

($P=0.031$).

Preoperative and 1-year follow-up memory outcomes are shown in Table 4. Multivariate ANOVAs revealed that the side of surgery had a significant effect on verbal memory preoperatively ($P=0.022$) but not significant on non-verbal memory and total memory preoperatively ($P>0.05$). Regarding left-side SeAH, verbal memory and total memory were increased significantly postoperatively ($P<0.05$) but non-verbal memory was not increased significantly ($P>0.05$), while, regarding left-side ATL, no significant increases were seen in verbal, non-verbal and total memory ($P>0.05$). In the right-side resections, verbal memory and total memory were increased significantly postoperatively in the 2 surgery strategy groups ($P<0.05$), and no significant increases were found in non-verbal memory in the 2 groups ($P>0.05$).

Table 2 Correlation of seizure control with clinical variables in medial temple lobe epilepsy ($n=72$)

Clinical variables	Class I and II/No.	Class III and IV/No.	Total/No.	<i>P</i>
Surgery side				0.131
Right	33	4	37	
Left	26	9	35	
Surgery strategy				0.760
ATL	28	5	33	
SeAH	31	8	39	
Pathology				0.033
Neoplasias or cavernous hemangioma	38	4	42	
Non-neoplasias	21	9	30	
Duration of history/year				0.165
<5	30	3	33	
5 to <10	12	5	17	
≥ 10	17	5	22	
Seizure frequency/month				0.522
<5	17	2	19	
5 to <20	23	7	30	
≥ 20	19	4	23	
Major seizure type				0.694
Auras	17	3	20	
Simple partial seizures	9	1	10	
Complex partial seizures	14	5	19	
Generalized seizures	19	4	23	

Table 3 Preoperative and follow-up IQ with medial temple lobe epilepsy ($n=72, \bar{x} \pm s$)

IQ test	Left-side			Right-side		
	Preoperative	Follow-up	P	Preoperative	Follow-up	P
Verbal IQ						
ATL	83.50±8.19	84.38±9.45	0.782	87.46±7.11	87.26±10.13	0.583
SeAH	81.58±5.23	85.23±8.48	0.021	86.86±9.81	89.13±9.23	0.048
Performance IQ						
ATL	89.16±8.89	89.88±10.12	0.672	90.13±8.18	91.12±9.37	0.835
SeAH	86.23±6.23	87.02±7.38	0.521	89.80±9.38	90.63±9.55	0.108
Full-scale IQ						
ATL	85.00±7.54	85.68±9.12	0.893	87.13±10.15	88.46±7.94	0.442
SeAH	84.82±5.49	87.35±8.92	0.031	87.72±9.86	89.18±8.99	0.152

Table 4 Preoperative and follow-up memory test with medial temple lobe epilepsy ($n=72, \bar{x} \pm s$)

Memory test	Left-side			Right-side		
	Preoperative	Follow-up	P	Preoperative	Follow-up	P
Verbal						
ATL	72.35±9.14	74.05±10.21	0.217	74.73±7.19	78.26±10.61	0.025
SeAH	69.94±8.25	72.85±7.76	0.047	75.81±6.62	78.81±9.14	0.034
Non-verbal						
ATL	82.56±8.44	83.72±10.10	0.230	79.67±7.89	83.53±10.14	0.092
SeAH	81.17±7.97	83.00±9.56	0.194	80.40±8.34	82.90±9.45	0.123
Total memory						
ATL	73.33±9.26	73.77±9.32	0.723	74.86±9.12	79.73±11.01	0.024
SeAH	71.41±8.18	76.64±9.26	0.001	76.13±6.90	79.95±8.73	0.011

3 Discussion

Surgical treatment of MTLE is an efficient and well-established method. ATL, always in combination with amygdalohippocampectomy, used to be the most widely performed standard resection^[13]. Further developments were the so-called “tailored resections” such as SeAH that aims at the resection of the suggested epileptogenic zone, in which surgery is restricted to the temporomesial structures in the presence of mesial pathology^[8, 14-15]. It was assumed that preserving more so-called “normal temporal cortex” by tailored resection may decrease the neuropsychological impairment. Today, many centers favor the tailored resections, like SeAH over standard ATL, especially in patients with a MRI-proven hippocampal sclerosis. However, there are conditions that may require additional resection of neocortical structures. That is, for example, in patients with dual pathology or when surface or intracranial EEG recordings indicates that the seizure

origin is not only limited to temporomesial parts of the temporal lobe.

Seizure outcome is one outcome variable to determine a better surgical approach. Clusmann et al^[16], in a retrospective study, compared the seizure outcomes of different strategies including SeAH, ATL (with amygdalohippocampectomy), purely lateral temporal lesionectomy, corticectomy or lesionectomy, and corticectomy plus additional hippocampectomy and found different strategies for surgery result in equally good seizure outcome. There is other evidence that seizure outcomes of ATL and SeAH do not differ^[8, 17]. In our experience, postoperative seizure control is not markedly different between patients who have undergone an ATL and those who have undergone SeAH. Thus, we might conclude that seizure outcome is not the relevant factor to prefer one over the other approach.

We analyzed the seizure control impact factors, and found that only the lesional pathology may affect the

seizure outcomes, others like the side of surgery, seizure frequency preoperative, main type of seizure, duration of symptom were not consider as seizure control impact factors. In our series, the patients with neoplastic lesion may underwent operation just after diagnosis, and this patients get good seizure outcomes partly because the seizure had not induced the peritumor zone to another epileptogenic zone.

Regard to neuropsychological outcome in MTLE, there is an ongoing discussion as to which surgical approaches may be optimized. Many studies reported superiority of SeAH compared with ATL in some aspects of postoperative cognitive performance, but some showed substantially mixed findings or lack of superiority of more limited resection. The comparison between two approaches is difficult because most centers usually perform one preferred procedure and comparison usually relies on the results reported by other centers. The completely controlled random trail in one center is needed.

In 1982, Wieser and Yaşargil^[6] found verbal memory deficits after left ATL but not after left SeAH and impairment in visual learning after right ATL but not after right SeAH. From then on, many authors reported that SeAH showed less cognitive impairment than ATL, at least in some part of memory function. Goldstein et al^[18] showed that left-sided surgery caused clear deterioration in verbal memory after both ATL and SeAH, but to a lesser extent in SeAH, and that right ATL produced more deterioration than right SeAH on non-verbal memory. According to the authors, SeAH produced a short-term beneficial effect on memory. Renowden et al^[19] found that patients who underwent left SeAH (transcortical or transsylvian) showed significant improvement in verbal IQ and non-verbal memory over those who underwent left ATL. Both surgeries resulted in a decline in verbal memory, suggesting that both left mesial and lateral temporal cortex contribute to verbal memory. In 59 patients with left MTLE and left lesional epilepsy, Helmstaedter et al^[20] reported that verbal memory did not change after cortical lesionectomy. In contrast, ATL and SeAH led to a significant deterioration in verbal memory, especially in recognition and free recall. However, different from SeAH and cortical resections, ATL led to a significant loss in total immediate recall 3 months after surgery. Thus, these

results indicate that not only lateral temporal cortex but also mesial structures contribute to immediate recall and recognition. Pauli et al^[21] found a significant loss in verbal memory in the left-sided ATL, and the efficiency of verbal retention was also markedly impaired after ATL compared with SeAH.

Patients with good verbal performance and a left-sided seizure focus preoperatively tended to exhibit deterioration after surgery; the rate of deterioration was significantly dependent on the resection type, and SeAH was found to be better than ATL on the left side regarding verbal memory^[16, 22]. Paglioli et al^[8] showed that left-sided SeAH caused significant improvement in verbal memory, but the same effect was not seen after right-sided resections. They stated that selective resection, especially transcortical SeAH, should be the choice of approach in patients with left MTLE. Morino et al^[15] showed no significant difference between the 2 surgical approaches with respect to IQ. Left-sided ATL and SeAH caused decline in verbal IQ and performance IQ, respectively. They found that ATL and SeAH produced verbal and non-verbal memory decline after left- and right-sided resections, respectively, and memory function overall was better preserved in patients undergoing SeAH.

However, Goldstein et al^[23] did not show differences with respect to memory 15 months after surgery. They underlined that there was no evidence that SeAH results in a less degree of everyday memory impairment than ATL. Some recent studies^[12, 24] also confirmed that ATL or SeAH can produce similar neuropsychological consequences.

In the present study, we provide clear evidence of different effects of left and right temporal resections on IQ performance and memory functions. In the right-side surgery, both SeAH and ATL showed no significant difference on postoperative IQ performance and memory outcomes. But, in the right-side surgery, SeAH showed favorite neuropsychological outcomes compared with ATL, including verbal IQ, full-scale IQ, verbal memory and total memory. The main limitation of the current study is that the trail is retrospective and not completely random control for the 2 groups. Further randomized studies ideally comparing SeAH with ATH, where improvements in certain aspects of verbal memory have been found and extended observational periods using a wider range of neuropsychological methods are needed.

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