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Predictors of meaningful improvement in quality of life after selective amygdalohippocampectomy in Chinese patients with refractory temporal lobe epilepsy: A prospective study

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ABSTRACT

Purpose: Our aim was to determine the independent predictors of minimum clinically important difference (MCID) in quality of life (QOL) after selective amygdalohippocampectomy (SAH) among Chinese patients with refractory mesial temporal lobe epilepsy (MTLE).

Methods: We conducted a prospective study and enrolled 50 consecutive patients with refractory MTLE who underwent SAH after their presurgical evaluations. The variables independently associated with MCID in the Quality of Life in Epilepsy Inventory-31 (QOLIE-31) overall score 1 year after SAH were analyzed by multiple binary logistic regression analysis.

Results: Significant improvements in the QOLIE-31 overall score and all subscale scores were observed after SAH ($p < 0.001$). Among 50 patients with refractory MTLE, 78% reached the criteria for MCID of QOL overall score after SAH. In the multiple binary logistic regression model, the presurgical independent predictors of significant improvement by MCID in QOL were absence of depression diagnosis (adjusted odds ratio [OR] = 8.391, 95% confidence interval [CI] = 1.240–56.776, $p = 0.029$) and good cognitive function (adjusted OR = 8.427, 95% CI = 1.115–63.670, $p = 0.039$); the postoperative independent predictor was seizure freedom (adjusted OR = 8.477, 95% CI = 1.195–60.122, $p = 0.032$). The sensitivity and specificity for significant improvement in the QOL were 97.4% and 45.5% respectively, with an overall model accuracy of 86.0%.

Conclusions: Presurgical depression, cognitive function, and postsurgical seizure freedom are independent predictors for meaningful improvement in QOL after SAH among the Chinese patients with refractory MTLE. Preoperative evaluation of patients with refractory MTLE should consider the cognitive dysfunction and psychological disorders.

1. Introduction

Epilepsy is one of the most common chronic neurologic disorders. Twenty to 30% of the patients with epilepsy (PWE) have uncontrollable seizures that are refractory to antiepileptic drugs (AEDs). For the patients who have been unable to alleviate seizures after at least 2 trials of AEDs, epilepsy surgery is widely accepted as an effective treatment, leading to seizure control in approximately 60–80% of the cases, particularly in the patients with mesial temporal lobe epilepsy (MTLE) [1–3]. Anterior temporal lobectomy (ATL) is considered as the standard surgical method for MTLE, with the proven safety and ability to control epileptic seizures [2,4,5]. However, there are associated potential risks with ATL that include cognitive deficits, such as attention, naming, and memory impairment [6]. Recently, advanced selective approaches have been developed to limit the deficits, of which the selective amygdalohippocampectomy (SAH) is one of the most controlled surgical options [7,8]. Compared with ATL, SAH has similar beneficial effects on seizure control with better cognitive outcomes among the patients with MTLE [9–11].

Epilepsy is considered to be strongly associated with a poor quality of life (QOL) [12]. Several factors have been associated with poor QOL in refractory MTLE, including uncontrolled seizures, age at onset, duration of epilepsy, side effects of AEDs, and comorbid conditions such as the presence of depressive and/or anxiety symptoms, and cognitive deficits [12,13]. A predominant objective of the epilepsy management is to improve the patient QOL to acceptable levels [14]. The effect of surgery on QOL has been shown to be significant [4]. Quality of life improved within 6 months after the surgery, regardless of seizure outcome. Seizure-free and aura-free status are the vital factors that impact the subsequent changes in QOL over time [15]. Even though there have been several studies investigating QOL before and after epilepsy

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surgery, and the statistical significance in the QOL scores might be included in these studies, significant changes with respect to what patients would consider to be meaningful changes were not taken into account [2,4,16]. The smallest difference in the score that patients perceive as important, either beneficial or harmful, and that would lead the clinician to consider a change in the patient's management is defined as the minimum important difference (MID) [17,18]. If a clinical trial demonstrates statistically significant changes in the QOL outcomes, the key question is the extent to which these results are clinically meaningful. Clinically meaningful results may be identified as a particular proportion of patients achieving a predefined degree of benefit [19]. The minimal clinically significant difference is the smallest difference that the clinicians and patients would consider to be essential for the epilepsy management. Correspondingly, the concept of minimum clinically important difference (MCID) has been developed to describe the smallest meaningful change in the scores that patients or clinicians would appreciate as clinically meaningful such that an intervention or treatment would be considered worthy of repeating [20–23]. Thus, MCID goes beyond the concept of statistical significance. Limited researches have applied the concept of MCID to predict the QOL after surgery [24]. Besides, there have been no relevant studies that investigate the presurgical assessments including psychological disorders and cognitive deficits to determine the independent predictors of clinically significant improvement in QOL after epilepsy surgery with the MCID concept.

In this study, we conducted a prospective study enrolling 50 consecutive patients with refractory MTLE, who underwent SAH during their presurgical evaluation to determine the independent predictors associated with MCID in the Quality of Life in Epilepsy Inventory-31 (QOLIE-31) overall score one year after the surgery. Furthermore, to our knowledge, this is the first study to determine the independent predictors of clinically significant improvement in the QOL after SAH in the Chinese population.

2. Methods

2.1. Study participants

Fifty patients with refractory MTLE who underwent SAH were enrolled consecutively during their presurgical evaluation between October 2016 and October 2018 at the Department of Functional Neurosurgery and Department of Neurology, Ruijin Hospital, affiliated to Shanghai JiaoTong University School of Medicine, China. This research was approved by the Ethics Committee of Ruijin Hospital in conformation with the Helsinki Declaration, Good Clinical Practice, and local regulations. Written informed consent was obtained from patients or legal guardians of the children before any trial-related procedures were performed.

According to the International League Against Epilepsy (ILAE), clinical characteristics of MTLE are classified into three forms: (1) simple partial seizures (SPS), involving retention of consciousness; (2) complex partial seizures (CPS), characterized by a disruption of normal awareness; and (3) secondarily generalized tonic–clonic seizures (GTCS) [25]. The inclusion criteria for the study were as follows: (1) medical history and seizure semiology consistent with MTLE, such as epigastric, autonomic, or psychic auras, followed by motor arrest, progressive clouding of consciousness, oroalimentary or manual automatisms, and autonomic phenomena; (2) a unilateral epileptic focus in the mesial temporal regions confirmed by prolonged video-electroencephalography (VEEG) monitoring; (3) refractory epilepsy defined by ILAE as failure of adequate trials of at least two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom, with seizures that impair awareness occurred at least once a month in the last 12 months [26]. The exclusion criteria were as follows: (1) epilepsy resulting from intracranial space-occupying lesions indicated by the magnetic resonance imaging (MRI) or other photographic results; (2) cardiopulmonary anomalies, progressive neurologic disorders, tumors, severe cognitive deficits, mental disease, or any other known disease that might affect the surgery and necessary evaluations; (3) suspected alcohol or drug addiction in 12 months preceding randomization of this study; and (4) history of noncompliance.

2.2. Presurgical and postsurgical evaluation

The presurgical and postsurgical evaluations were completed by the same team, composed of neurologists, neurophysiologists, neuropsychologists, and psychiatrists. All patients had completed a standardized presurgical diagnostic evaluation including epilepsy characteristics, seizure semiology and monthly frequency, age at epilepsy onset, duration of epilepsy, monthly frequency of seizures impairing awareness, side of temporal abnormality, medication, and comorbidities. The presurgical demographic characteristics such as gender, age, occupation, and years of education were documented in our study. According to a standardized epilepsy protocol, ictal and interictal VEEG monitoring and MRI were combined to discover the structural lesions [27]. Magnetoencephalography (MEG) was performed in all the patients as a part of preoperative evaluation to determine the epileptogenic foci precisely. Invasive EEG recordings with depth and/or subdural electrodes were performed if necessary. Histopathology was carried out for all the patients in the specimens collected during the surgical process. Hippocampal sclerosis was diagnosed by hippocampal atrophy on T1 and fluid-attenuated inversion recovery (FLAIR) and increased hippocampal signal on T2 MRI and FLAIR sequences, as well as the histological neuronal cell loss and gliosis [28].

Neurologic examination and psychiatric and neuropsychological assessments were performed and were blinded to the QOLIE-31 assessments. All the patients were assessed by the experts during the presurgical evaluation and 12 months after SAH. The neuropsychological and psychiatric assessments usually sustained for about one to 2 h. Scales analyzed in our study included Hamilton Depression Scale (HAMD), Self-rating Anxiety Scale (SAS), Self-rating Depression scale (SDS), Mini-mental State Examination (MMSE), and Montreal Cognitive Assessment (MoCA). The HAMD score of 8 or higher suggests depression [29,30]. The SAS and SDS are self-report questionnaires with 20 items rating the burden of anxiety and depression. Scores of each item range from 1 to 4, and the total score on each questionnaire is multiplied by 1.25. Total SAS score of more than 50 points indicates anxiety symptoms, and total SDS score of more than 53 categorized individuals as suffering from depression [31]. The MMSE and MoCA score of 24 was used as a cutoff for good cognition as it has been shown that this score exhibited sensitivity and good specificity in the detection of mild cognitive impairment [32,33]. All the patients were interviewed alone first and thereafter, together with the caregivers.

2.3. Evaluation of QOL and determination of MCID

Quality of life was evaluated with the Chinese version of the QOLIE-31 during the presurgical evaluation and 12 months after SAH. The QOLIE-31 is an epilepsy-specific questionnaire that evaluates QOL in PWE that has been used and validated internationally [27,34,35] and is composed of 7 subscales: overall QOL, seizure worry, emotional well-being, energy/fatigue, cognitive and medication effects, and social function. According to the QOLIE-31 scoring manual, values responded by the patients are converted to 0–100 scores to generate seven individual scores corresponding to seven subscales and one total score. The higher values of subscales and total scores in QOLIE-31 indicate a better QOL.

Determination of MCID can be calculated by statistical or clinical methods [22]. As a result of the absence of patient-centered changes to estimate MCID clinically, we adopted a distribution-based statistical method. The statistical method compared the changes in QOLIE-31 overall and subscale scores before and after SAH. Generally, one standard deviation (SD) calculated from the mean QOLIE-31 overall score before epilepsy surgery was considered as MCID. The same approach was also applied to determine the MCID for each of the seven scores of the QOLIE-31 subscales.

2.4. Surgical procedure and routine postsurgical follow-up

After integrating the clinical characteristics, electrophysiological tests, and imaging examinations, also taking into account the functional weightiness and the potential risks for neurologic deficits induced by the resection, surgical decision and concrete procedures were made by the same team of experienced surgeons. Epilepsy surgery was completed at the Department of Functional Neurosurgery, Ruijin Hospital. Administration of AED after SAH in accordance with presurgical schedule was emphasized to all the patients and their caregivers repeatedly. Routine postsurgical follow-up was done 12 months after surgery by the neurosurgical team. Postsurgical frequency of seizures and surgical complications were well documented.

2.5. Statistical analysis

Statistical Package for Social Sciences (SPSS) software version 24.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses. Differences between presurgical and postsurgical QOLIE-31 scores and neuropsychological assessments were analyzed by paired t-test or Wilcoxon's signed-rank test. On the basis of MCID criteria adopted in our study, differences between the clinical characteristics, demographic, presurgical QOLIE-31 scores, neuropsychological and psychiatric states, and QOL improvement after SAH were analyzed by univariate binary logistic regression. In order to determine the independent predictors for meaningful improvement in QOL one year after SAH, differences between variables showing an association with QOL improvement for a p level <0.10 in the univariate analysis and QOL improvement after SAH were analyzed by multiple binary logistic regression. p-Values of <0.05 were considered to be statistically significant.

Table 1
Demographic and clinical characteristics of patients before surgery (n = 50).

Parameter	Value
Total no. of patients	50
Gender	
Male	30 (60%)
Female	20 (40%)
Frequency of seizures (n/months)	10.08 ± 9.93
Seizure type	
SPS	1 (2%)
CPS	28 (56%)
Secondarily GTCS	21 (42%)
Work activity	
Unemployed	16 (32%)
Employed	34 (68%)
Education (years)	9.46 ± 2.76
Age at surgery(years)	27.04 ± 9.86
<25 years	22 (44%)
≥25 years	28 (56%)
Age at seizure onset (years)	15.32 ± 10.41
<10 years	13 (26%)
≥10 years	37 (74%)
Disease duration(years)	11.72 ± 7.65
<10 years	23 (46%)
≥10 years	27 (54%)
No. of current AEDs	1.82 ± 0.77
Monotherapy	20 (40%)
Two or three AEDs	30 (60%)
History of adverse AED reactions	12 (24%)
Site of seizure focus	
Left	23 (46%)
Right	27 (54%)
Etiology	
FCD	10 (20%)
HS	34 (68%)
Others	6 (12%)

Values expressed as mean ± SD or as number (%).
AEDs: antiepileptic drugs; HS: hippocampal sclerosis; SPS: simple partial seizures; CPS: complex partial seizures; GTCS: generalized tonic–clonic seizure; FCD, focal cortical dysplasia.

3. Results

3.1. Characteristics of the study population

All the patients were diagnosed with refractory MTLE. None manifested psychiatric disorders or severe depression or anxiety that might interfere with surgical procedures or postsurgical follow-up. All the patients had support from their families. The average age at the time of surgery was 27.04 years, and the average age of seizure onset was 15.32 years. Thirty participants (60%) were male. About half of our patients (46%) were diagnosed with lesions in the left hemisphere. The seizure frequency before surgery was 10.08 ± 9.93 (average ± SD) times a month, and 21 (42%) patients suffered from secondarily GTCS. Twenty patients (40%) were on monotherapy, and thirty patients (60%) were on polytherapy during the presurgical evaluation. Twelve patients (24%) had a history of adverse AED reactions. Thirty-four of our patients (68%) confirmed hippocampal sclerosis. Sixteen patients (32%) were conducted with invasive EEG recordings. Demographic data and clinical characteristics are listed in Table 1.

There were no irreversible surgical complications or visual field deficits that happened objectively or were complained by the participants throughout our study. A slight skin infection in the surgical wound happened in one patient, which was successfully cured with antibiotics. The seizure outcomes were defined based on Engel classifications [36]. In the routine postsurgical follow-up, 12 months after SAH, freedom from seizures occurred in 37 patients (74%), which was defined as Engel class I (no seizures or auras); seven patients (14%) had less than three seizures in a year (Engel class II), and six (12%) patients had more than three seizures in a year (Engel class III or IV). The current AEDs used before surgery in mono or in combined polytherapy were carbamazepine (n = 19), oxcarbazepine (n = 17), valproate (n = 15), levetiracetam (n = 14), topiramate (n = 10), phenytoin (n = 6), lamotrigine (n = 6), phenobarbital (n = 2), or clonazepam (n = 2).

3.2. Predictors independently associated with MCID in the QOLIE-31

The presurgical and postsurgical QOLIE-31 overall scores and subscale scores, and scores of MMSE, MoCA, SAS, SDS, and HAMD respectively are shown in Table 2. There were significant improvements in all the QOLIE-31 total and subdomain scores assessed 12 months after SAH ($p < 0.0001$). Significant improvements were observed in MoCA, SAS, SDS, and HAMD scores as well. After comparing each subscale of MoCA, three different domains of cognition including the visuospatial/executive, naming, and abstraction showed significant improvements after SAH. However, we did not find a significant improvement in MMSE scores one year after epilepsy surgery.

According to the statistical method used to estimate the MCID, one SD calculated from the mean QOLIE-31 scores before epilepsy surgery was set as MCID. Therefore, a change of 16.47 points in QOLIE-31 overall score was determined as significant improvement in our study, which is similar to that previously reported [14,21,22]. The numbers and percentage of patients reaching to the criteria for MCID in QOLIE-31 overall score 1 year after SAH are shown in Table 3. Seventy-eight percent of patients attained the MCID of 16.47 points, hence, grouped as patients with significant improvement. Likewise, the same approach was also applied to determine the MCID for each of the seven scores of QOLIE-31. None of our patients got worse in QOLIE-31 overall score or in the seven subscale scores as per the MCID criteria. Table 3 shows in detail the numbers and percentage of patients achieving various levels of MCID in QOLIE-31 seven subscales.

Table 2
Scaled scores of overall QOLIE-31 and its subscales, MMSE, MoCA, SAS, SDS, and HAMD before and after surgery.

Parameter	Before	After	p value*
QOLIE-31	51.54 ± 16.47	72.08 ± 13.00	<0.001*
Seizure worry	38.04 ± 27.15	74.30 ± 16.46	<0.001*
Overall QOL	61.55 ± 18.04	81.25 ± 14.19	<0.001*
Emotional well-being	49.52 ± 14.62	68.57 ± 15.09	<0.001*
Energy and fatigue	57.80 ± 16.83	73.69 ± 20.27	<0.001*
Cognitive function	53.39 ± 26.33	71.55 ± 21.78	<0.001*
Medications effects	60.32 ± 29.40	82.33 ± 18.25	<0.001*
Social function	44.24 ± 27.50	65.93 ± 23.04	<0.001*
MMSE	25.08 ± 5.80	25.58 ± 4.82	0.062
MoCA	20.98 ± 6.18	22.10 ± 5.74	0.001*
Visuospatial/executive	3.24 ± 1.20	3.42 ± 1.05	0.005*
Naming	2.66 ± 0.59	3.42 ± 1.05	0.002*
Attention	4.90 ± 1.72	5.06 ± 1.20	0.114
Language	2.02 ± 0.94	1.96 ± 0.88	0.577
Abstraction	0.94 ± 0.68	1.48 ± 0.65	0.003*
Delayed recall	2.22 ± 1.80	2.30 ± 1.84	0.578
Orientation	5.22 ± 1.18	5.22 ± 1.20	1.000
SAS	38.36 ± 11.43	33.42 ± 11.81	0.006*
SDS	46.14 ± 13.16	37.66 ± 12.24	<0.001*
HAMD	9.72 ± 8.50	7.76 ± 4.87	0.010*

Values expressed as mean ± SD.
* $p < 0.05$ was considered as significant.

The results of univariate binary logistic regression analyses for predictors of QOL improvement after SAH are shown in Table 4. A strong correlation was observed between MCID and presurgical depression diagnosis evaluated by both SDS (OR = 0.067, 95% CI = 0.012–0.366, p = 0.001) and HAMD (OR = 0.155, 95% CI = 0.029–0.813, p = 0.037). A strong correlation between MCID and postsurgical seizure freedom (OR = 9.625, 95% CI = 2.136–43.364, p = 0.003) was also demonstrated. Furthermore, we established a significant association between QOL improvement and better cognition by MMSE (OR = 0.176, 95% CI = 0.039–0.801, p = 0.030) and MoCA (OR = 0.124, 95% CI = 0.024–0.658, p = 0.014). We then analyzed the relationship between subscale scores of MoCA and significant improvement in QOL. As shown in Supplementary Table 1, there were no statistically significant differences observed in the changes in subscale scores of MoCA.

In the next multiple binary logistic regression analyses, we included the variables showing an association with QOL improvement one year after SAH with a p level <0.10 in the univariate analyses. As shown in Table 5, the absence of presurgical depression diagnosed by both SDS and HAMD (adjusted OR = 8.391, 95% CI = 1.240–56.776, p = 0.029), presurgical good cognition by MoCA (adjusted OR = 8.427, 95% CI = 1.115–63.670, p = 0.039), and postoperative seizure freedom (adjusted OR = 8.477, 95% CI = 1.195–60.122, p = 0.032) was still significantly associated with QOL improvement to MCID, showing an overall model accuracy of 86.0%, with 97.4% specificity and 45.5% sensitivity.

Table 3
The proportion of patients achieving various levels of change in QOLIE-31 overall score 1 year after SAH.

QOLIE-31	Score change	MCID in the QOLIE-31 after epilepsy surgery		
		Decline, n(%)	No-change, n(%)	Improve, n(%)
Overall score	±16.47	0(0)	11(22)	39(78)
Seizure worry	±27.15	0(0)	12(24)	38(76)
Overall QOL	±18.04	0(0)	11(22)	39(78)
Emotional well-being	±14.62	0(0)	14(28)	36(72)
Energy and fatigue	±16.83	0(0)	23(46)	27(54)
Cognitive function	±26.33	0(0)	28(56)	22(44)
Medications effects	±29.40	0(0)	30(60)	20(40)
Social function	±27.50	0(0)	33(66)	17(34)

4. Discussion

Patients with refractory epilepsy, whose seizures fail to achieve full control with more than two trials of AEDs, should be recommended an epilepsy surgery according to the established guidelines [37,38]. In our study focused on Chinese patients with refractory MTLE, significant improvements in the QOL overall and subscale scores were demonstrated one year after epilepsy surgery. Our results are consistent with several previous studies where QOLIE-31 or other QOL-related instruments were applied [16,39,40]. Judging by the MCID criteria, we established a clinically significant improvement in QOL after epilepsy surgery in the Chinese patients with refractory epilepsy, in agreement with the recent studies conducted in Canadian, Swedish, and Brazilian populations [14,22,41].

Among all the presurgical and postsurgical variables analyzed in the Chinese patients, the absence of depression diagnosis, good cognition in the presurgical evaluation, and a complete seizure control after SAH was found to be independently associated with MCID in the QOL after the multiple binary logistic regression analyses.

Although it is widely accepted by the clinicians that seizure frequency could be a dominating predictor of QOL in PWE after epilepsy surgery, previous studies have indicated that only seizure freedom, rather than a reduction in frequency of seizures, is associated with better QOL after surgery [16,42]. It has also been confirmed that seizure freedom is indispensable to persistent improvement in QOL in the first two years after epilepsy surgery [15,43,44]. The effectiveness of neurosurgery in drug-resistant MTLE for seizure control is well established [2,4,5]. The standard procedure is ATL, which consists of removing a part of the anterior area of the lateral temporal lobe and the underlying medial structures, including hippocampus and amygdala. In order to limit the extent of resection and possibly minimize postsurgical complications, SAH, in which only the medial temporal structures are removed, may also be conducted as an alternative. Even though the meta-analyses by Josephson et al. [45] and Hu et al. [46] demonstrated that ATL increased the likelihood of achieving control from disabling seizures, defined as Engel class I;, most studies have not identified a significant difference in seizure outcome between the ATL and SAH. A recent meta-analysis study published in 2018, which included the most articles, showed no difference in seizure-free outcome of ATL versus SAH [10]. An 18-year follow-up after the surgery for TLE also found that SAH or ATL did not impact the seizure outcome [47]. Besides, all 50 consecutive patients received SAH in our study, thus, we can exclude the effect of the surgical technique (ATL or SAH) on seizure-free outcome and QOL.

The prevalence of depression in patients with recurrent seizures ranges from 20% to 55%, prominently higher than that in patients with controlled epilepsy ranging from 3% to 9%, and that of 4.7% globally [48,49]. Patients with partial epilepsy are more vulnerable to depression compared with patients with generalized epilepsy while MTLE is the most common cause of partial seizures [50,51]. Psychological disorders might serve as more reliable determinants of a declining QOL than seizure frequency [52]. The HAMD score was one of the strong predictors of QOL in the Chinese PWE [35]. In our study, the presurgical depression was a determinant of QOL improvement after SAH according to both depression questionnaires. According to ILAE Psychology Task Force, evidence-based recommendations indicate that psychological treatment should be taken into consideration among PWE with psychological comorbidities to improve the QOL [53]. The impact of psychiatric treatment before SAH on postsurgical QOL is worthy of further investigations.

Cognitive deterioration is estimated to occur in approximately 70–80% of PWE [54], which could increase the disability in PWE, particularly in those with refractory MTLE [53]. Poor cognitive outcome is generally relevant for a few factors, such as uncontrolled seizures, AEDs, an early onset, a long disease duration, and reduced effective connectivity in the brain [54] while the exact pathogenesis of cognitive deterioration is still

Table 4
Univariate binary logistic regression analyses for predictors of QOL improvement after SAH.

Predictive variables	All cases, n (%)	QOL improvement, n (%)		Crude OR (95% CI)	p-Value
		Yes	No		
Sex					
Male	30 (60.00)	24 (80.00)	6 (20.00)	1.333 (0.345, 5.147)	0.736
Female	20 (40.00)	15 (75.00)	5 (25.00)		
Age					
<25 years	22 (44.00)	18 (81.82)	4 (18.18)	1.500 (0.377, 5.965)	0.734
≥25 years	28 (56.00)	21 (75.00)	7 (25.00)		
Work activity					
Unemployed	14 (28.00)	10 (71.43)	4 (28.57)	0.603 (0.145, 2.505)	0.476
Employed	36 (72.00)	29 (80.56)	7 (19.44)		
Site of seizure focus					
Left	23 (46.00)	18 (78.26)	5 (21.74)	1.029 (0.268, 3.942)	1.000
Right	27 (55.00)	21 (77.78)	6 (22.22)		
Etiology					
HS	35 (70.00%)	29 (82.86)	6 (17.14)	2.417 (0.603, 9.678)	0.269
NO-HS	15 (30.00%)	10 (66.67)	5 (33.33)		
Education					
<9 years	13 (26.00)	10 (76.92)	3 (23.08)	0.920 (0.203, 4.159)	1.000
≥9 years	37 (74.00)	29 (78.38)	8 (21.62)		
AEDs					
Monotherapy	20 (40.00)	14 (70.00)	6 (30.00)	0.467 (0.120, 1.810)	0.311
Two or three AEDs	30 (60.00)	25 (83.33)	5 (16.67)		
Depression (SDS)					
Yes	18 (36.00)	9 (50.00)	9 (50.00)	0.067 (0.012, 0.366)	0.001*
No	32 (64.00)	30 (93.75)	2 (6.25)		
Depression (HAMD)					
Yes	25 (50.00)	16 (64.00)	9 (36.00)	0.155 (0.029, 0.813)	0.037*
No	25 (50.00)	23 (92.00)	2 (8.00)		
Anxious (SAS)					
Yes	7 (14.00)	5 (71.43)	2 (28.57)	0.662 (0.110, 3.991)	0.641
No	43 (86.00)	34 (79.07)	9 (20.93)		
MMSE					
<24	10 (20.00)	5 (50.00)	5 (50.00)	0.176 (0.039, 0.801)	0.030*
≥24	40 (80.00)	34 (85.00)	6 (15.00)		
MoCA					
<24	23 (46.00)	14 (60.87)	9 (39.13)	0.124 (0.024, 0.658)	0.014*
≥24	27 (54.00)	25 (92.59)	2 (7.41)		
Disease duration					
<10 years	23 (46.00)	16 (69.57)	7 (30.43)	0.398 (0.100, 1.587)	0.305
≥10 years	27 (54.00)	23 (85.19)	4 (14.81)		
Age at epilepsy onset					
<10 years	13 (26.00)	12 (92.31)	1 (7.69)	4.444 (0.510, 38.739)	0.248
≥10 years	37 (74.00)	27 (72.97)	10 (27.03)		
Seizures/month					
<4	15 (30.00)	12 (80.00)	3 (20.00)	1.185 (0.267, 5.264)	1.000
≥4	35 (70.00)	27 (77.14)	8 (22.86)		
History of secondarily GTCS					
Yes	21 (42%)	15 (71.43)	6 (28.57)	0.521 (0.135, 2.011)	0.491
No	29 (58%)	24 (82.76)	5 (17.24)		
Seizure control after SAH					
Seizure-free	37 (74.00)	33 (89.19)	4 (10.81)	9.625 (2.136, 43.364)	0.003*
Seizure	13 (26.00)	6 (46.15)	7 (53.85)		

AED: antiepileptic drug; HS: hippocampal sclerosis; GTCS: generalized tonic–clonic seizure.
* $p < 0.05$ was considered as significant.

uncertain [55,56]. Memory deterioration is the most common cognitive deficit in PWE, reported in approximately 20% to 30% of the patients [57]. Furthermore, about 80% of the patients with MTLE report the origin of the disease in the hippocampus [58] while hippocampal sclerosis is the main etiology in surgical patients. The MoCA scale is a convenient cognitive screening tool to detect cognitive impairment with relatively high specificity and sensitivity [32]. It is more sensitive than other cognitive scales with regard to abnormal manifestation across multiple domains, such as verbal and visuospatial memory and naming, which represent domains that are more specifically related to temporal lobe function, and thus, widely applied in various neuropsychiatric disorders [59]. Several researchers have suggested MoCA scale as a screening evaluation for PWE [60]. Our study was the first to suggest the presurgical cognitive function as the independent predictor of QOL significant improvement after epilepsy surgery. A better cognitive function before the surgery might reflect a better functional reserve of the contralateral temporal lobe that determines postoperative cognition and hence, affects the QOL. Because of the fact that each subscale score was not more than 6 points and the changes were minor, we have failed to analyze the relationship between the subscale scores and significant

Table 5
Multiple regression analyses for the variables independently associated with MCID after SAH.

QOLIE-31 overall score predictors	Adjusted OR (95% CI) for improvement	p-Value
No presurgical depression	8.391 (1.240, 56.776)	0.029*
Good cognition	8.427 (1.115, 63.670)	0.039*
Seizure-free after surgery	8.477 (1.195, 60.122)	0.032*
Specificity (%)	97.4	
Sensitivity (%)	45.5	
Overall accuracy (%)	86.0	

improvement in QOL. However, a larger sample size could establish a possible association, which needs further investigation.

A trend that the patients with more psychological symptoms are more susceptible to the neurocognitive deficits has been observed [61]. In addition to the surgical intervention, neuropsychological evaluations should be routinely administered to PWE before an epilepsy surgery that can, thus, provide relevant prognosis for the epilepsy management. Clinically, cognitive-behavioral therapy and mood-based interventions have consistently demonstrated significant effects on the improvement of QOL [62]. Another potential implication of our findings is that QOL after epilepsy surgery in PWE might be improved by presurgical behavioral or pharmacological interventions targeting psychiatric comorbidities and neurocognitive deficits.

This is the first prospective study to date that evaluates the presurgical psychological and cognitive assessments to determine the independent predictors of clinically significant improvement in QOL after epilepsy surgery with the concept of MCID. Moreover, rare studies have applied the multivariate analyses to investigate the predictors of QOL after epilepsy surgery. With an advantage to control confounding variables associated with QOL scores, multivariate analyses are particularly useful to determine the variables that can independently predict the QOL after epilepsy surgery in the patients with MTLE [14,27]. There were also limitations in our study. Firstly, we evaluated a relatively small sample size ($n = 50$), which might conceal the precise associations between presurgical and postsurgical variables with the MCID of the QOLIE-31 overall score. Thus, our findings are preliminary and should be replicated with a larger sample size in future studies. Secondly, a one-year follow-up is a relatively short period of time, thus, QOL might improve or worsen after 12 months. However, existing studies have shown that the postsurgical QOL is already stable 6 months after surgery during a long-term follow-up of more than one year [15].

5. Conclusion

The current study in the Chinese patients with refractory MTLE indicates that the presurgical depression and cognition status, as well as the postsurgical seizure freedom, are independent predictors for meaningful improvement in QOL after SAH, and provides the guidance for the presurgical evaluations and treatments. We believed that preoperative evaluations of the patients with refractory MTLE should consider the psychological disorders and cognitive deficits.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2019.05.006.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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