



## Risk factors for suicidal tendency in adult patients with epilepsy in China

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### ABSTRACT

**Objective:** The major cause of premature mortality in people with epilepsy (PWE) is suicide. Actual data on the risk of suicidal tendency in adult PWE in China are scarce. In our study, associations between possible risk factors and suicidal tendency in adult PWE in China were investigated.

**Methods:** People with epilepsy ( $n = 251$ ) were recruited, and their demographic and clinical characteristics were evaluated. Suicide risk was examined using the suicidality module (SM) of the Mini International Neuropsychiatric Interview (MINI) Plus Chinese Version 5.0.0.

**Results:** Suicidal tendency was present in 36 (14.3%) of the 251 PWE. On the basis of the results of univariate analyses, family relationship ( $P < 0.001$ ), age at epilepsy onset ( $P = 0.037$ ), seizure-free period ( $P = 0.041$ ), seizures/month ( $P = 0.015$ ), depressive disorders ( $P < 0.001$ ), and number of antiepileptic drugs (AEDs) ( $P = 0.017$ ) were associated with suicidal tendency. Multivariate analysis revealed that moderate or poor family relationships (odds ratio (OR): 6.468, 95% confidence interval (CI): 2.418–17.300) and depressive disorders (OR: 3.548, 95% CI: 1.575–7.995) were associated with high odds of suicidal tendency.

**Conclusion:** Suicidal tendency is common among adult PWE. This study reveals that family relationships and depressive disorders are independent risk factors for suicidal tendency among adult PWE. Therefore, while maintaining treatment of epilepsy, more attention should be directed to the social support and mental state of PWE to prevent suicide.

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### 1. Introduction

Epilepsy is a common chronic brain disease that has become a major public health issue worldwide. Previous studies have reported that suicide is more common in people with epilepsy (PWE) than in people without epilepsy. A large, population-based, case–control study from Denmark between 1981 and 1997 used five nationwide registries to obtain information about epilepsy, showing that of the over 21,000 people who committed suicide, 2.3% had a history of epilepsy compared with 0.7% of the 420,000 controls, which means PWE were three times more likely to commit suicide than people without a history of epilepsy [1]. In a retrospective study from Taiwan, the epilepsy and comparison cohorts included 68,543 patients and twice as many controls, respectively and found that the epilepsy cohort had a 2.06-fold higher risk of suicide ideation (95% confidence interval (CI) = 1.65–2.56) compared with the control cohort [2].

It seems obvious that PWE have a higher risk of suicide than people in the general population. Before the completed suicidal act, there are three phases that people will go through. The three phases are suicidal ideation, suicide plan, and suicide attempt, which can be used to evaluate the risk of suicidal tendency. The data show that 25% of PWE have a lifetime history of suicidal thoughts, and more than 10% have a suicide attempt at least once in their lifetime [3]. It is very difficult to predict death caused by suicide because of methodological problems. However, suicidal tendency is a significant warning sign for suicide, and there are many ways to screen for this tendency. Ascertaining the suicidal tendency of PWE and identifying the association between risk factors and suicidal tendency may be critical for preventing PWE from committing suicide.

A large body of evidence has shown that medical disorders are a risk factor for both suicidal ideation and death by suicide. Particularly, the majority of patients with suicidal ideation or who died by suicide were clinically depressed. Previous research has found that depression, previous mood disorders, a prior history of medical disorders, and cognitive impairment are the most important risk factors for suicide [4]. In general, the coexistence of psychiatric comorbidities is highly prevalent in PWE, which may lead to decreases in the quality of life as well as may be an important clinical correlate of suicide [5]. However, it remains

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unclear whether epilepsy itself or psychiatric comorbidities lead to suicide in PWE. Several studies have shown a link between risk of suicide and temporal lobe epilepsy, lack of aura before seizure, high seizure frequency, female sex, and socioeconomic status [6,7]. We can presume that if suicidal tendency in adult PWE is mainly associated with seizure-related factors, we should treat the epilepsy itself to prevent suicide. However, if psychiatric factors are independent risk factors for suicidal tendencies, we should focus on managing the patient's psychiatric problems, which can lessen the risk of suicide.

In Asia, China is a developing country whose society, economy, and culture differ significantly from those of other countries, and information regarding suicide risk and epilepsy is scarce. This study aimed to investigate the role of sociodemographic characteristics and seizure-related variables in suicidal tendency in adult patients with epilepsy in China.

## 2. Methods

### 2.1. Subjects

The study included 251 patients with epilepsy who were part of a follow-up observation project at the specialized epilepsy clinic of the First Affiliated Hospital of Wenzhou Medical University, China. In all studies, patients were consecutively recruited from October 2018 to January 2019 and assessed with the same clinical instruments, which are described in more detail in the subsequent sections. The inclusion criteria were as follows: 1. patients were 16–80 years old with a current diagnosis of epilepsy according to International League Against Epilepsy (ILAE) criteria; 2. patients were willing to provide informed consent to participate and agreed to the aims and protocols of the study. Patients were excluded if they had the following conditions: 1. mental retardation or serious neurological or psychiatric disorders, 2. refusal to respond to the questionnaires or unable to understand the questionnaire, and 3. incomplete medical record information.

### 2.2. Ethics statement

The Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University provided approval for the study, and informed consent was obtained from all patients.

### 2.3. Data collection

A total of 258 patients with epilepsy were included in the study. Two patients were excluded because the diagnosis of epilepsy was questionable. Patients with epilepsy with incomplete medical records from which we could not acquire sufficient clinical data were also excluded ( $n = 5$ ). The final group consisted of 251 patients with epilepsy. Each subject was interviewed by trained epileptologists who also extracted sociodemographic data and epilepsy-related clinical information from the Wenzhou Epilepsy Follow-Up Registry Database (WEFURD). The details of the WEFURD were introduced in a previous publication [8].

### 2.4. Questionnaires

The Mini International Neuropsychiatric Interview (MINI) Plus Chinese Version 5.0.0 is a brief, simple structured psychiatric diagnostic interview based on the Diagnostic and Statistical Manual of Mental Disorders/International Classification of Diseases (DSM/ICD) criteria [9]. The suicidality module (SM) of the MINI Plus includes six questions that pertain to the “wish for death”. The top five questions focus on current suicidal ideation, suicide plan, and suicide attempt within the past 4 weeks. The last question concerns lifetime suicide attempts. The degree of current suicidality is based on a weighted point system that classifies the risk as low (score = 1–5), medium (score = 6–9), or high (score  $\geq 10$ ). The Chinese version of this instrument has been validated

[10]. In our study, 251 patients with epilepsy were categorized into two groups on the basis of SM scores: having suicidality ( $n = 36$ ) or absent suicidality ( $n = 215$ ).

### 2.5. Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS version 20.0, SPSS Inc., Chicago, IL, USA). Sociodemographic characteristics and clinical variables are presented as counts, frequency (%), means, and standard deviations. Continuous variables were compared using Student's *t*-tests, and categorical variables were compared using chi-square tests or Fisher's exact tests. The threshold for statistical significance was set at  $P < 0.05$  (two-tailed). Factors associated with suicidal tendency in PWE were measured by logistic regression analyses.

## 3. Result

The study sample consisted of 251 adult patients with epilepsy: 55.4% were male, and the mean age was 34.61 years (Standard Deviation (SD): 11.29), which ranged from 16 to 76 years old. According to the SM of the MINI, 36 (14.3%) fulfilled the criteria for suicidality risk, including 23 at a low level (score = 1–5), 10 at a moderate level (score = 6–9), and 3 at a high level (score  $\geq 10$ ). Among the 36 PWE, 21 (58.3%) had suicide attempts determined by answering “yes” to the last question, “Have you ever attempted suicide?” Table 1 shows the details of the sociodemographic characteristics of the suicide risk group and nonsuicide risk group. Subjects of the two groups who were single, divorced, or widowed were classified as “unstable marital status”, and “unemployed” occupational status included those who were retired, unemployed, and students. Education time was divided into 0–9 years (finished primary school), 9–12 years (graduate from the junior middle school), 12–16 years (graduate from senior high school), and more than 16 years (university graduated). The economic factor was classified as follows: annual household income less than 50,000 RMB/year, 50,000–100,000 RMB/year, and more than 100,000 RMB/year. According to univariate analysis, family relationships were significantly associated with suicidal tendency ( $P < 0.001$ ), while sex, age, stable marital

**Table 1**  
Comparison of sociodemographic characteristics between two groups of PWE.

Demographic variables	With suicidal risk (n = 36) (%)	Without suicidal risk (n = 215) (%)	P-value
Sex			
Male	20 (55.6)	119 (55.3)	
Female	16 (44.4)	96 (44.7)	0.982
Age (SD) (years)	32.47 (8.2)	34.96 (11.7)	0.408
Stable marital status			
Yes	19 (52.8)	139 (64.7)	
No	17 (47.3)	76 (35.4)	0.172
Education time (years)			
0–9	5 (13.9)	31 (14.4)	
9–12	17 (47.2)	90 (41.9)	
12–16	6 (16.7)	44 (20.5)	
>16	8 (22.2)	50 (23.3)	0.93
Occupational status			
Employed	22 (61.1)	142 (66)	
Unemployed	14 (38.9)	73 (34.1)	0.565
Faith			
Yes	21 (58.3)	116 (54)	
No	15 (41.7)	99 (46)	0.625
Family relationship			
Good	24 (66.7)	198 (92.1)	
Moderate/poor	12 (33.4)	17 (7.9)**	<0.001
Annual household income (ten thousand yuan)			
<5	13 (36.1)	72 (33.5)	
5–10	14 (38.9)	82 (38.1)	
>10	9 (25.0)	61 (28.4)	0.924

\*\*  $P < 0.01$ .

status, education time (years), occupational status, faith, and annual household income shown in Table 1 had no statistically significant association with suicidal tendency ( $P > 0.05$ ).

Table 2 shows the association between suicidal tendency and clinical characteristics. Diagnosis of depressive disorders was made by experienced neurologists. Every PWE was examined using the Hamilton Depression Scale-17 (HAMD-17). A total score above 7 corresponded to a depressive disorder. The risk factors of suicidal tendency were revealed by univariate analyses of our findings. The mean age at onset of epilepsy in the suicide risk group was 18.65 years, compared with the nonsuicide risk group with a mean age at onset of 23.57 years ( $P = 0.037$ ); mean age at onset of epilepsy was significantly correlated with suicidal tendency. In addition, according to the results of univariate analysis, seizure-free period ( $P = 0.041$ ), seizure frequency per month ( $P = 0.015$ ), and depressive disorders ( $P < 0.001$ ) were associated with suicidal tendency. There was no association between suicide and seizure-inducing factors, mean duration of epilepsy, type of seizure and epilepsy, epileptic focus, etiology or electroencephalogram (EEG) findings (within 3 months).

Table 3 compares the association of therapy with six common types of antiepileptic drugs (AEDs) (valproate, carbamazepine, lamotrigine, levetiracetam, topiramate, and oxcarbazepine) and suicidal tendency between the two groups. In our findings, the number of AEDs ( $P =$

**Table 2**  
Comparison of clinical characteristics between two groups of PWE.

Variables	With suicidal risk (n = 36) (%)	Without suicidal risk (n = 215) (%)	P-value
Mean age at onset of epilepsy (SD) (years)	18.65(10.0)	23.57(12.9) *	0.037
Mean duration of epilepsy (years)			
<1	1 (2.8)	6 (2.9)	
1–5	11 (30.6)	65 (30.2)	
6–10	4 (11.1)	46 (21.4)	
11–20	10 (27.8)	63 (29.3)	
>20	10 (27.8)	34 (15.8)	0.358
Inducing factor			
No	33 (91.7)	190 (88.4)	
Yes	3 (8.4)	25 (11.6)	0.404
Seizure-free period (years)			
>2	4 (11.1)	58 (27.0)	
0–2	32 (88.9)	157 (73.0) *	0.041
Seizure frequency per month			
0–1	27 (75.0)	186 (86.5)	
>1	9 (25.0)	19 (13.5) *	0.015
Type of seizure			
FES	12 (33.3)	50 (23.3)	
2nd GES	21 (58.3)	146 (67.9)	
GES	3 (8.3)	19 (8.8)	0.413
Type of epilepsy			
Cryptogenic	8 (22.2)	53 (24.7)	
Symptomatic	25 (69.4)	152 (70.7)	
Idiopathic	3 (8.3)	10 (4.7)	0.612
Epileptic focus			
Not focal	5 (13.9)	36 (16.7)	
Focal, extratemporal	17 (47.2)	92 (42.8)	
Focal, temporal	14 (38.9)	87 (40.5)	0.855
Etiology			
Structural/metabolic	16 (44.4)	72 (33.5)	
Others	20 (55.6)	143 (66.5)	0.139
Depressive disorders			
No	16 (44.4)	160 (74.4)	
Yes	20 (55.6)	55 (25.6) **	$P < 0.001$
EEG (within 3 months)			
Normal	10 (27.8)	59 (27.4)	
Abnormal but without epileptiform abnormalities	5 (13.9)	19 (8.8)	
Abnormal with epileptiform abnormalities	20 (55.6)	124 (57.7)	
No EEG	1 (2.8)	13 (6.0)	0.714

FES, focal epileptic seizure; GES, generalized epileptic seizure.

\*  $P < 0.05$ .

\*\*  $P < 0.01$ .

**Table 3**  
Comparison of the use of antiepileptic drugs between two groups of PWE.

Variable	With suicidal risk (n = 36) (%)	Without suicidal risk (n = 215) (%)	P-value
Conventional AEDs			
Valproate			
No	23	164	
Yes	13	51	0.114
Carbamazepine			
No	33	183	
Yes	3	32	0.294
New AEDs			
Lamotrigine			
No	24	171	
Yes	12	44	0.086
Levetiracetam			
No	23	135	
Yes	13	80	0.9
Topiramate			
No	29	189	
Yes	7	26	0.346
Oxcarbazepine			
No	21	108	
Yes	15	107	0.368
No. of AEDs			
1	7 (19.4)	68 (31.6)	
2	8 (22.2)	75 (34.9)	
$\geq 3$	21 (58.3)	72 (33.5) *	0.017

AEDs, antiepileptic drugs.

\*  $P < 0.05$ .

0.017) was associated with suicidal tendency. However, there was no association between suicidal tendency and the use of particular types of AEDs.

Finally, the factors associated with suicidal tendency in PWE were included in the multivariable analysis. The results indicated that family relationships (odds ratio (OR): 6.468, 95% CI: 2.418–17.300) and depressive disorders (OR: 3.548, 95% CI: 1.575–7.995) were associated with higher odds of suicidal tendency (Table 4).

#### 4. Discussion

Compared with similar studies in other countries, our study revealed some differences. In this study, 14.3% of the PWE had some degree of suicidal tendency, which is lower than previous studies showing 25%–30% in a population-based analysis in Canada and in Korea [7,11]. One possible explanation is that we chose the SM of the MINI as the screening criteria to screen for PWE with suicidal tendency. We directed more

**Table 4**  
Multivariate analysis comparing risk factors associated with suicidality in PWE.

Variable	OR (95% CI)	P-value
Family relationship		
Good	1.000 (reference)	
Moderate/poor	6.468 (2.418–17.300) **	<0.001
Mean age at onset of epilepsy (years)	0.972 (0.935–1.011)	0.153
Seizure-free period (years)		
>2	1.000 (reference)	
0–2	0.567 (0.163–1.966)	0.371
Seizure frequency per month		
–1	1.000 (reference)	
>1	1.637 (0.609–4.396)	0.329
Depressive disorder		
No	1.000 (reference)	
Yes	3.548 (1.575–7.995) **	0.002
No. of AEDs		
1	1.000 (reference)	
2	0.886 (0.275–2.862)	0.840
$\geq 3$	1.773 (0.603–5.216)	0.298

CI, confidence interval; OR, odds ratio.

\*\*  $P < 0.01$ .

attention to the current suicidal tendency of PWE. Some PWE had suicidal ideations in the past; however, suicide did not occur. Based on the characteristics of the SM of the MINI, we could not identify this group of patients. In addition, this was hospital-based research, and most PWE are able to keep their seizures and depressive disorders under control with medical treatment. Another reason may be the differences in interethnicity and culture, as Chinese usually have higher tolerance for chronic disease.

Our research found that poor family relationships could greatly increase the risk of suicide attempt and was associated with a 5.011-fold increase in the OR of suicide. Seizure has a significant impact on the quality of life of patients, which is manifested in physiological, psychological, and social functions and other aspects. Many PWE are unable to lead normal lives. As a chronic disease, epilepsy is paroxysmal and unpredictable. Patients with epilepsy always have the risk of either becoming unconscious or falling and hurting themselves. This easily brings about social discrimination, leading to patients with decadence, low self-esteem, and even negative views of society [12]. Epilepsy sometimes is linked with outdated, insensitive, and preposterous views that tend to be stigmatizing. Stigma is often viewed as an attribute that is greatly demeaning. To avoid being stigmatized, some PWE, as well as their families, are forced to reject the label of epilepsy. The moral burden attached to epilepsy not only affects PWE but also their families when people consider epilepsy to be genetic [13]. Good support from relatives and friends is required for PWE to understand their disease correctly, and access to appropriate and timely caring services is necessary.

In most studies on suicide, psychiatric disorders are the primary clinically relevant factor. The incidence of depression in patients with epilepsy is higher than that in patients with other neurological diseases [14]. According to a recent meta-analysis, the incidence of depression in PWE is 22.9% [15]. As expected, depressive disorders were significantly associated with suicidal tendencies in our study. In the current study, the incidence of depressive disorder in PWE was 29.9%, higher than in previous data. This study considered depressive disorders rather than depression. We found that depressive disorders were associated with a 3.088-fold increase in the OR of suicide. It is notable that in this study, 44.4% of the PWE with suicidal tendency did not have accompanying depressive disorders, which suggests that the risk of suicide should be evaluated separately when the psychological aspects of patients with epilepsy are assessed. Because even patients without depressive disorders, the possibility of suicidal tendency cannot be excluded.

The clinical characteristics that were assessed included seizure-related variables, including mean age at onset of epilepsy, mean duration of epilepsy, seizure-inducing factors, seizure-free period, seizure frequency per month, type of seizure, type of epilepsy, epileptic focus, etiology, AED polytherapy, EEG, and depressive disorders. Previous studies have reported one or more of the above variables to predict suicidality in PWE. However, there was a lack of available evidence, or only weak associations had been reported between the frequency of seizures or AED polytherapy and suicide attempts [16]. In this study, there was no statistically significant difference between the two groups based on the seizure-related variables. However, epileptic-related factors may cause depressive disorders, which may lead to suicidal tendencies. The relationship between epilepsy itself and depression is complex, and previous studies have shown different results. Perini and Mendius [17] found that the lateralization of epileptogenic lesions had an effect on depression while Swinkels et al. [18] found no differences between symptoms of depression in patients with the lateralization of epilepsy in the left versus the right hemisphere. Zis et al. [19] found that seizure control is an important determinant of a major depression risk among PWE while Pereira and Valente [20] found that the severity of depressive symptoms was not correlated with age, sex, seizure control, age at onset, duration of epilepsy, and the presence of hippocampal sclerosis in children. From the above results, we can conclude that to prevent

suicide, while maintaining the treatment of epilepsy, more attention should be directed to the mental state of PWE.

In 2008, the Food and Drug Administration issued an alert based on the results of a meta-analysis of placebo-controlled clinical trials of 11 AEDs, which suggested that there was an increased risk of suicide ideation and behavior among people whose seizures are being treated with AEDs. There were some limitations in this study due to methodological difficulties and the lack of information regarding the state of seizure control, and therefore, the research findings remain controversial [21]. Some research has reported that gamma-aminobutyric acid energy drugs, including phenobarbital, vigabatrin, tiagabine, and topiramate, can provoke or worsen depression [22]. Compared with treatment with other AEDs, levetiracetam in PWE was associated with a higher risk of completed suicide [6]. We also examined the relationship between AEDs and suicidality. The chi-square analysis revealed that AED polytherapy was significantly associated with suicidality ( $P < 0.05$ ) while the logistic regression analysis did not identify the number of AEDs as a predictor. We did not demonstrate a harmful effect of any particular type of AED on suicidal tendency. In our study, 37.1% of our patients used 3 or more types of AEDs, which may have led to AED interactions and attenuated the overall effect of a single AED on mood or suicidal tendency.

This study has some limitations, and our results should be considered while bearing in mind the following. First, our finding was based on a relatively small sample; therefore, the data need to be interpreted with caution, and a larger sample in future studies is needed. Second, this analysis was a cross-sectional study based in a specialized epilepsy clinic of a tertiary academic hospital, and the subjects are adults. Therefore, our results may not be representative of the general population of PWE, especially adolescents or teenagers who are more likely to exhibit suicidal ideations and attempt suicide [2,23,24]. Third, psychiatric disorders are an important clinical correlate of suicide [6], but our study considered only depressive disorders. Therefore, future studies should be conducted to establish the impact of other psychiatric disorder factors on suicidal tendency.

## 5. Conclusions

There is a lack of actual and comprehensive data on the risk of suicidal tendency in adult patients with epilepsy in China. Our study fills in the gaps and finds that suicidal tendency is common among adults with epilepsy. The suicidal tendency of adult PWE is mainly associated with family relationships and depressive disorders rather than seizure-related variables. Neurologists and other clinicians should focus on managing the psychiatric problems of PWE, assess whether PWE have adequate social support, and help them eliminate self-isolation with appropriate medical therapy. In particular, we strongly recommend that clinicians use rapid suicidality screening instruments among PWE with relevant risk factors, which can lessen the risk of suicide.

## Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

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