Focal Points of the Preanesthesia Evaluation for Electroconvulsive Therapy in Patients with Depression: A Retrospective Analysis of Clinical Characteristics in Nonremission

Lei Zou

First Affiliated Hospital of Chongqing Medical University

Xiao Li

First Affiliated Hospital of Chongqing Medical University

Qibin Chen

First Affiliated Hospital of Chongqing Medical University

Feng Lv

First Affiliated Hospital of Chongqing Medical University

Su Min (✉ ms89011068@163.com)

First Affiliated Hospital of Chongqing Medical University

Research Article

Keywords: ECT, retrospective analysis, nonremission, depression

Posted Date: January 19th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1220765/v1>

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Abstract

Background: This study explored the patient clinical characteristics that may affect electroconvulsive therapy (ECT) efficacy, to enable improved focus during the evaluation and preparation before ECT.

Methods: Patients enrolling for ECT at the Department of Psychiatry and Anesthesiology of the First Affiliated Hospital of Chongqing Medical University from December 2017 to January 2019. Univariate and multivariate analyses were performed to identify the risk factors for nonremission. Variables with statistical significance in the univariate analysis were included in the multivariate logistic regression analysis to determine independent risk factors.

Results: In total, 874 cases showed efficacy in this study. After ECT treatment, 255 cases (29.2%) exhibited nonremission. Multivariate logistic regression analysis of variables was performed, and the results showed that atherosclerosis (OR 8.072, 95% CI 2.442 to 16.675; $p = 0.001$), COPD (OR 2.919, 95% CI 1.240 to 6.871; $p = 0.014$), diabetes (OR 2.202, 95% CI 1.115 to 4.348; $p = 0.023$) and smoking (OR 1.519, 95% CI 1.015 to 2.273; $p = 0.042$) were independent risk factors for nonremission.

Conclusion: In the retrospective analysis, we found that atherosclerosis, diabetes, COPD or smoking may be high-risk factors for nonremission.

Introduction

Depression is a mood disorder characterized by persistent feelings of loss of interest along with a cluster of clinical symptoms. The World Health Organization projects that worldwide, depression will be the leading cause of disease burden by 2030, and depression is a significant public health concern affecting 350 million people worldwide^{1, 2}. Despite the development of newer brain stimulation techniques and novel pharmacological agents, no treatment has approached the efficacy of electroconvulsive therapy (ECT) for depression, especially for patients whose medical or psychiatric condition requires a rapid and/or definite response³, and researchers have been trying to identify other methods to improve the efficacy of ECT.

Anesthesia is an indispensable part of ECT treatment, as it not only eliminates the patients' fear of the procedure, thereby reducing the stress response, but also reduces the incidence of adverse events, such as fracture, tooth injury, and cardiovascular and cerebrovascular accidents. Furthermore, the rational use of anesthetics such as propofol and ketamine can improve the efficacy of ECT^{4–6} and may confer at least a short-term advantage in terms of improving depressive symptoms at the early stages of ECT⁷. A series of studies conducted by our research group also supported these views^{8, 9}.

We studied the effects of ketamine in different age groups and confirmed its validity and safety. At the same time, by referring to the literature, we found that ECT was particularly effective in elderly individuals with depression^{10–12}. However, there are differing views. Some studies have suggested that response and remission rates to pharmacotherapy and ECT are not sufficiently different between old-age and middle-

age depression to be clinically significant¹³ or that effectiveness is independent of age¹⁴. In addition, elderly individuals may have more complications, such as hypertension, diabetes, atherosclerosis, and hyperlipidemia, which may aggravate the depressive symptoms of the patients^{15–17}.

Combined with our research and current reports, we believe that patient age, medical complications, adjuvant anesthesia and other factors will affect the treatment of ECT and may be the reasons why depression is not alleviated after treatment with ECT. However, there is no comprehensive analysis of these factors. Therefore, the purpose of this study was to explore the risk factors that may affect the efficacy of ECT so that the anesthesia can be adjusted accordingly.

Methods

This study retrospectively included patients who enrolled for ECT at the Department of Psychiatry and Anesthesiology of the First Affiliated Hospital of Chongqing Medical University from December 2017 to January 2019. The study protocol was approved by the ethics committee of the hospital, and all aspects of the study complied with the Declaration of Helsinki. There is no need to obtain informed consent from patients since this is a retrospective study, and all the data were collected and analyzed anonymously.

The inclusion criteria were complete medical records, and subjects diagnosed with depression (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) were included. We excluded patients diagnosed with other psychiatric diseases. We collected clinical data of patients through the electronic medical record system. Basic information on the patients, such as age, sex, body mass index (BMI), smoking history, drinking history, course of disease, marital status, and recurrent depression, was collected. Education level was divided into illiterate, nine-year compulsory education and high school, and above. Smoking status was classified as nonsmoking and smoking. Additionally, participants were divided into a nondrinking group and a drinking group. Marital status was classified as unmarried, married, divorced and widowed. According to age, participants were classified as minor (<18 years), youth (18–44), middle age (45–59) and old age (≥ 60 years). The physical examination included measurements of height and weight. We measured height and weight to the nearest 1 cm and 0.1 kg, respectively. BMI was calculated as the weight in kilograms divided by the height in meters squared. Individuals with BMIs ≥ 24 kg/m² were considered to be overweight, and those with BMIs ≥ 28 kg/m² were considered to be obese. Complications included diabetes, hypertension, atherosclerosis, hyperlipidemia, chronic obstructive pulmonary disease (COPD), and hypothyroidism. Outpatients were excluded because of incomplete information.

Depressive symptoms were assessed using the 24-item Hamilton Depression Rating Scale (HAMD-24) at baseline and after the end of the ECT session. Response was defined as a $\geq 50\%$ decrease in HAMD-24 scores from baseline. Remission was defined as a HAMD-24 score ≤ 10 after the last two consecutive ECT sessions.

Statistical analyses were performed using IBM SPSS Statistics 26.0 software (IBM Corporation, Armonk, NY). Univariate and multivariate analyses were performed to identify the risk factors for nonremission. The Shapiro-Wilk test was used to determine whether the course of disease and number of treatments were normally distributed. All measurement data are presented as the mean $\pm$ SD (standard deviation) when data met the criteria for normality with $p > 0.10$. Otherwise, the data are presented as the median (interquartile range, IQR). When the data met the criteria for normality and homogeneity of variance, statistical analysis between groups was performed using independent samples t-tests. Otherwise, measurement data with a nonnormal distribution were analyzed by means of the Mann-Whitney U test. Variables with statistical significance in the univariate analysis were included in the multivariate logistic regression analysis to determine independent risk factors. p values < 0.05 were considered statistically significant.

Results

During this period, 1617 patients received ECT, of which 903 were diagnosed with depression. Because not all the information could be obtained for outpatients, 874 inpatients were included. According to the diagnostic criteria, 619 patients achieved remission, with a remission rate of 70.8%. A total of 255 people did not reach the remission standard, accounting for 29.2% of the patients (Fig. 1, Table 1).

Table 1 General condition of patients with depression after ECT [cases (%)]		
Total	remission	nonremission
874 (100)	619 (70.8)	255 (29.2)

None of the patients had severe complications. Their clinical features are shown in Table 2, and the results of the univariate analyses are also included. The results showed that there were no significant differences in remission rates among participants according to sex ($P=0.774$), education ($P=0.304$), alcohol use ($P=0.199$) and family history of depression ($P=0.687$). There were significant differences in age ($P=0.003$), hypertension ($P=0.002$), diabetes ($P=0.000$), marital status ($P=0.018$), BMI ($P=0.018$), smoking ($P=0.014$), atherosclerosis ($P=0.000$), COPD ($P=0.005$), hyperlipidemia ($P=0.000$), hypothyroidism ($P=0.038$), history of anesthesia ($P=0.014$), first-onset depression ($P=0.004$), course of depression ($P=0.000$), and number of ECTs ($P=0.000$) (Table 2, Table 3).

Table 2. Univariate analyses of the risk factors for nonremission

	remission (n=619)		nonremission (n=255)		χ^2	p
Age(year)					14.093	0.003*
<18	111	17.9%	29	11.4%		
18-44	289	46.7%	109	42.7%		
45-59	145	23.4%	66	25.9%		
≥ 60	74	12.0%	51	20.0%		
Gender					0.083	0.774
male	217	35.1%	92	36.1%		
famale	402	64.9%	163	63.9%		
Marital status					10.318	0.018*
unmarried	257	41.5%	79	31.0%		
married	321	51.9%	150	58.8%		
divorced	28	4.5%	19	7.5%		
widowed	13	2.1%	7	2.7%		
Education					2.379	0.304
illiterate	29	4.7%	16	6.3%		
9-years compulsory education	321	51.9%	119	46.7%		
high school or above	269	43.5%	120	47.1%		
BMI					8.030	0.018*
<18.5	20	3.2%	5	2.0%		
18.5-23.9	565	91.3%	223	87.5%		
≥ 24	34	5.5%	27	10.6%		
Smoking					6.100	0.014*
yes	89	14.4%	54	21.2%		
no	530	85.6%	201	78.8%		
Alcohol use					1.647	0.199
yes	88	14.2%	45	17.6%		
no	531	85.8%	210	82.4%		
Diabetes					13.863	0.000*

yes	22	3.6%	25	9.8%		
no	597	96.4%	230	90.2%		
Hypertension					9.169	0.002*
yes	43	6.9%	34	13.3%		
no	576	93.1%	221	86.7%		
Atherosclerosis					25.586	0.000*
yes	4	0.6%	16	6.3%		
no	615	99.4%	239	93.7%		
Hyperlipidemia					13.416	0.000*
yes	27	4.4%	28	11.0%		
no	592	95.6%	227	89.0%		
COPD					7.893	0.005*
yes	12	1.9%	14	5.5%		
no	607	98.1%	241	94.5%		
Hypothyroidism					4.301	0.038*
yes	27	4.4%	20	7.8%		
no	592	95.6%	235	92.2%		
History of anesthesia					5.979	0.014*
yes	156	25.2%	85	33.3%		
no	463	74.8%	170	66.7%		
Family history of depression					0.163	0.687
yes	94	15.2%	36	14.1%		
no	525	84.8%	219	85.9%		
First-onset depression					8.231	0.004*
yes	238	38.4%	72	28.2%		
no	381	61.6%	183	71.8%		

Table 3. Univariate analyses of the risk factors for nonremission (continued)

	remission (n=619)	nonremission (n=255)	Z	P
Course of depression(month)	15 (5,48)	36 (8,75)	-24.099	0.000*
Number of ECT	10 (8,12)	9 (7,12)	-28.031	0.000*

Multivariate logistic regression analysis of variables with $P < 0.05$ was performed, and the results showed that atherosclerosis, COPD, diabetes and smoking were independent risk factors for nonremission. It can be seen from the data that the number of patients with these clinical characteristics who had nonremission increased by 8.072-, 2.919-, 2.202- and 1.519-fold, respectively (Table 4, Fig. 2).

Table 4. Multivariate analyses of the risk factors for nonremission

	<i>B</i>	<i>OR (95% CI)</i>	<i>P</i>
Age			
minors		1.000 (reference)	0.778
youth	0.145	1.156 (0.675-1.979)	0.597
middle age	0.105	1.111 (0.562-2.198)	0.762
old age	-0.119	0.888 (0.398-1.978)	0.771
Marital status			
unmarried		1.000 (reference)	0.629
married	-0.096	0.909 (0.575-1.436)	0.682
divorced	0.343	1.409 (0.685-2.900)	0.352
widowed	-0.012	0.988 (0.318-3.070)	0.983
BMI			
<18.5		1.000 (reference)	0.273
18.5-23.9	0.462	1.588 (0.559-4.510)	0.385
≥24	0.859	2.361 (0.728-7.660)	0.152
Smoking			
no			
yes	0.418	1.519 (1.015-2.273)	0.042*
Diabetes			
no			
yes	0.789	2.202 (1.115-4.348)	0.023*
Hypertension			
no			
yes	0.167	1.181 (0.652-2.140)	0.583
Atherosclerosis			
no			
yes	2.088	8.072 (2.442-16.675)	0.001*
Hyperlipidemia			
no			

yes	0.627	1.872 (0.991-3.539)	0.053
COPD			
no			
yes	1.071	2.919 (1.240-6.871)	0.014*
Hypothyroidism			
no			
yes	0.496	1.643 (0.865-3.121)	0.129
History of anesthesia			
no			
yes	0.346	1.414 (0.992-2.016)	0.055
First-onset depression			
no			
yes	0.257	1.293 (0.912-1.833)	0.148
Course of depression	0.002	1.002 (1.000-1.004)	0.075
Number of ECT	-0.127	0.881 (0.834-0.930)	0.000*

Discussion

At present, research on improving the efficacy of ECT is carried out mainly by psychiatrists in terms of aspects such as electroshock mode, electric quantity and stimulation site¹⁸, while anesthesiologists are concerned mainly with the different anesthetic compounds or administration modes^{19, 20}. By analyzing the clinical characteristics of nonremission patients, this study intended to improve the evaluation and regulation of patients before anesthesia to further improve the efficacy of ECT. We found that atherosclerosis, diabetes, COPD and smoking may be high-risk factors for nonremission ECT. To date, there is no relevant research, but it is certain that these factors will affect the symptoms of depression.

There is an interactive relationship between depression and atherosclerosis. Studies have shown that depression increases the risk of atherosclerosis. First, from the perspective of pathophysiology, depression is accompanied by immune dysregulation²¹, and in this context, the levels of a variety of peripheral inflammatory biomarkers are increased²². On the other hand, there are alterations in the nitric oxide (NO) system²³. Endothelium-derived NO, through its vasodilator properties, participates in the modulation of vascular tone²⁴. These factors promote atherosclerosis. In addition, the behavioral effects of depressive symptoms are considered to be another source of subclinical atherosclerosis, such as sleep disorders, sedentary behavior and obesity, smoking and alcohol consumption. Sleep disorders lead to

impaired vascular endothelial function²⁵, sedentary behavior causes intimal thickening of arteries²⁶, and smoking and obesity lead to the formation of atherosclerotic plaques²⁷, all of which contribute to an increased atherosclerotic burden. Depression and atherosclerosis have a common pathophysiological basis^{28, 29}, and it has been confirmed that intracranial atherosclerosis will aggravate the symptoms of depression³⁰. It has been reported that depression patients with atherosclerosis have a poor response to drug treatment³¹. However, ECT treatment has not been reported. Our study found that atherosclerosis is the most important reason for nonremission after ECT, showed that atherosclerosis may have an impact on depression in another way, and indicated that it will influence the treatment efficacy. Some studies have shown that the treatment of atherosclerosis can reduce depression³². Therefore, we should treat atherosclerosis when evaluating such patients, as this may improve the efficacy of ECT.

Evidence has also suggested a bidirectional relationship between diabetes and depression^{33, 34}. Numerous studies have confirmed that the course of depression in patients with diabetes is more severe and that depression episode relapses are more frequent. From a pathophysiological perspective, depression is highly consistent with diabetic complications. These complications include macrovascular complications (such as coronary artery disease), microvascular complications (diabetic retinopathy, neuropathy, nephropathy or end-stage renal disease) and bidirectional complications (depression may increase the risk of diabetic complications). On the other hand, these complications also affect the occurrence and development of depression^{17, 35}. Our research also shows that diabetes is a high-risk factor affecting the efficacy of ECT, which may be related to the aggravation of depressive symptoms by diabetic complications. The treatment of diabetes can reduce the symptoms of depression³⁶, which may help to improve the efficacy of ECT. However, there is still a lack of prospective studies to support this conclusion.

Our study also found that COPD and smoking are key indicators affecting the efficacy of ECT. These two factors are different from the previous two high-risk factors. Although they do not directly cause vascular disease, they affect the development of depression in other ways. COPD causes hypoxia by destroying the lung capillary bed and causing poor airway ventilation, leading to a decrease in neurotransmitter serotonin activity and eventually depression^{37, 38}. Hypoxia may also cause global suppression of cerebral metabolism (energy production), leading to depression^{39, 40}. A series of symptoms of COPD are also causes of depression, and dyspnea, as the core symptom of COPD, may play an important role in the causal relationship between COPD and depression^{41, 42}. These patients are less active, have a lower quality of life and have a worse mood. Smoking has an impact on vascular disease and lung disease, aggravating these diseases^{43, 44}. Smoking may also be an independent risk factor for depression^{45, 46}. This may be the reason why smoking affects the efficacy of ECT.

Treatment with these risk factors can improve the depressive symptoms of patients, but the correlation between these factors and ECT has not been reported. In addition, psychiatrists can improve the efficacy of ECT by changing the stimulation power, using different stimulation sites, and changing the stimulation

mode, among other actions^{18, 47, 48}. Therefore, we hope that when anesthesiologists evaluate patients, they will pay attention to and address these risk factors to further improve the efficacy of ECT.

Limitations

There were several limitations in this study. First, although these risk factors certainly have an effect on depression, we were unable to confirm their direct relationship with the risk of nonremission. Second, we could not rule out interactions between these factors. Third and most importantly, at present, there is a lack of prospective studies to confirm these findings. Therefore, in the next phase of the study, we will use the experience of enhanced postoperative recovery (ERAS) to treat depression patients who have these risk factors during the anesthesia evaluation.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (No.20140409) and a waiver of informed consent was granted. The study was carried out in accordance with Helsinki declaration.

Consent for publication

Not Applicable.

Competing interests

Authors have no conflicts of interest to report.

Funding

This work was supported by the National Natural Science Foundation of China grant (81271501), as well as a grant from National Key Clinical Special Construction Project (No.2011-170).

Author contributions

Lei Zou made statistics and wrote the manuscript. Su Min designed the research experiments. Qibin Chen helped with data collection. Xiao Li helped with data collection and ECT assessment. Feng Lv helped with data collection and made statistics.

Acknowledgments

The authors thank Xiaoni Zhong and Jing Zhao, Professors of Chongqing Medical University, for their constructive comments during the review process. We also thank Yao Gan, Associate Professor in the

Department of Psychiatry of the First Affiliated Hospital of Chongqing Medical University, for her helpful comments.

Data availability statements

The datasets generated during the current study are not publicly available due to involving patient privacy but are available from the corresponding author on reasonable request.

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Figures

Figure 1

Clinical research flow chart

Figure 2

Multivariate analyses of the risk factors for nonremission