

# Risk factors for malnutrition in refractory convulsive status epilepticus

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## Research

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# Abstract

**Purpose:** To study the risk factors and prognosis of malnutrition in patients with refractory convulsive status epilepticus.

**Methods:** A total of 73 patients with refractory convulsive epileptic status in West China Hospital from January 2017 to May 2019 were collected. All patients met the 2016 International Anti-epileptic Alliance diagnostic criteria for refractory convulsive status epilepticus. A logistic regression model was used to evaluate the risk factors of malnutrition in refractory convulsive status epilepticus.

**Results:** Of the 73 patients with refractory convulsive status epilepticus, 33 (45.21%) suffered from malnutrition during hospitalization, and hospitalization days (OR =1.251; 95% CI: 1.067-1.384; P =0.007), nasal feeding (OR =22.623; 95% CI: 1.091-286.899; P =0.013), and malnutrition on admission (OR =30.760; 95% CI: 1.064-89.797; P =0.046) were risk factors for malnutrition in patients with refractory convulsive status epilepticus.

**Conclusion:** Malnutrition is a common complication during hospitalization in patients with refractory convulsive status epilepticus. Hospitalization days, nasal feeding, and malnutrition at admission are risk factors for malnutrition in patients with refractory convulsive status epilepticus. Further longitudinal studies are needed to identify the relationship between refractory convulsive status epilepticus and adverse outcomes.

## Background

Convulsive status epilepticus is one of the most common critical and severe neurological diseases[1,3,7]. Its main feature is continuous epileptic seizure, with high disability and death rates, while refractory convulsive status epilepticus (RCSE) has higher complication and death rates[3-4,8]. Previous studies have shown that RCSE requires intravenous injection of narcotic drugs after regular treatment for patients with convulsive status epilepticus, accounting for 23%-48% of convulsive status epilepticus[3-4,8]. The fatality rate is as high as 23%-61%, which is 3 times as high as that of nonrefractory convulsive status epilepticus[3-4,5,8]. Malnutrition is a common complication during the hospitalization of patients with RCSE and may be related to poor prognosis. Malnutrition is usually defined as malnutrition caused by insufficient intake, poor absorption or excessive loss of nutrients, resulting in physical and mental functional defects[9]. A large number of studies show that the nutritional status of patients will deteriorate continuously during hospitalization. Despite receiving nutritional support, various nutritional parameters are still on a downward trend, and this decrease in nutrition may be related to the poor prognosis of patients[9-13]. The risk factors of malnutrition in patients with RCSE during hospitalization have not yet been reported. The nutritional status of the patients is evaluated at the time of admission; it may be important for treatment to discover the risk of malnutrition as soon as possible. Therefore, this study aims to explore the risk factors and prognosis of malnutrition in patients with RCSE during hospitalization to develop strategies and purposeful early interventions and to improve the prognosis.

# Research Methods

## Research Object

This study included 73 cases of RCSE patients from the NICU, Neurology and other departments in West China Hospital from January 2017 to May 2019. The diagnosis of all patients met the latest diagnostic criteria of the International Anti-epilepsy Alliance (ILAE)[1-2]. According to the standards of the Helsinki Declaration, this study strictly abided by the principle of patient's willingness and knowledge. If the patient did not have conscious autonomy, the willingness and knowledge of his immediate family members were obtained.

**Inclusion criteria:** 1. Age  $\geq 18$  years old; 2. Conform to the latest diagnostic standard of RCSE of the ILAE[1]  Voluntary and informed consent.

**Exclusion criteria:** 1. Age  $\leq 18$  years old; 2. No informed consent; 3. Primary psychosis or serious anxiety and depression disorder; 4, Liver cirrhosis or renal insufficiency and a need to limit protein intake; and 5. Hospitalization days fewer than 2 weeks.

## Research methods

According to the inclusion and exclusion criteria, the general patient data (including demographic information, hospitalization time and expenses) included serum albumin detected within 36 hours of admission and at the time of discharge, collected retrospectively; height and weight; body mass index (BMI); clinical characteristics at admission (including whether there is consciousness disorder, dysphagia, diet reduction, stress ulcer and nutritional status, etc.); and dysphagia status, i.e., the ability of the patient to drink 30 ml of water in the sitting position. Results Classification: Grade 1 is smooth swallowing, no choking coughs or pauses. Grade 2 consists of swallowing twice without choking coughs or pauses or prolonged to more than 5 s; Level 3 indicates being capable of swallowing once but with a choking cough. Grade 4 is divided into more than two swallows but still with a choking cough; Grade 5 is frequent choking cough, and a full swallow is difficult[22-23]. Dysphagia is considered to exist if the symptoms of dysphagia are present and if the drinking water test is  $\geq 3$  grade or there is consciousness disorder[22]. The Glasgow score is used for the evaluation of consciousness level.

**Nutritional status assessment:** nutritional status assessments were carried out by special personnel 24 hours after admission and discharge, including measurements of body weight and height and calculation of body weight index (BMI)  BMI = body weight (kg)/height (m<sup>2</sup>). The indexes of serum albumin, serum transferrin and serum prealbumin were detected. The Mini Nutrition Assessment Form (MNA) was completed[16]. Diagnostic criteria for malnutrition: meet  $\geq 1$  of the following 4 criteria: (1) BMI < 18.5 kg/m<sup>2</sup>; (2) serum albumin concentration < 35 g/l; (3) weight loss at discharge was greater than 6% of the weight at admission; Mna < 17. An MNA score of 17-23.5 indicates the risk of malnutrition[9-10].

## Data statistics and analysis

An SPSS 22.0 logistic regression model was mainly used for the statistical data. Fisher's exact test was used for counting data. Measurement data are expressed as the means and standard deviations ( $\bar{x}$  s). The measurement data were tested by t-test. Multivariate logistic regression analysis was carried out on the factors with statistical significance in single-factor analysis.  $P < 0.05$  was considered to have statistical significance.

## Results

A total of 33 out of 73 patients with RCSE were malnourished. There was no significant difference between the demographics of 33 patients with malnutrition (16 males, age  $39 \pm 21$  years) and 40 patients without malnutrition (28 males, age  $40 \pm 20$  years).

Patients suffering from malnutrition have longer hospitalization time, more hospitalization expenses and lower body weight and albumin when discharged from the hospital than patients without malnutrition.

The causes of 73 cases of RCSE include acute central nervous system infection (30 cases), head trauma (3 cases), brain tumor (7 cases), acute cerebrovascular disease (5 cases), ischemic anoxic encephalopathy (4 cases), other central nervous system abnormalities (7 cases), electrolyte acid-base imbalance (6 cases), and poor drug withdrawal/compliance (11 cases). The causes of 33 cases of malnutrition include central nervous system infection (15 cases), head trauma (1 case), brain tumor (4 cases), acute cerebrovascular disease (2 cases), ischemic anoxic encephalopathy (1 case), other central nervous system abnormalities (2 cases), electrolyte acid-base imbalance (4 cases), and poor drug withdrawal/compliance (4 cases).

There were 7 patients (9.59%) with malnutrition at the time of admission, including 4 patients with BMI  $< 18.5 \text{ kg/m}^2$  and 3 patients with albumin  $< 35 \text{ g/l}$ . There were 33 malnourished patients (45.21%) at the time of discharge, including 15 patients with weight loss greater than 6% of their body weight at the time of admission, 18 patients with BMI  $< 18.5 \text{ kg/m}^2$ , 19 patients with albumin  $< 35 \text{ g/l}$ , 33 patients with MNA  $< 17$  points, and 11 patients with MNA  $\geq 17$ -23.5 points. The incidence of malnutrition at discharge was significantly higher than that at admission (all  $p < 0.05$ ). The ratio of serum albumin  $< 35 \text{ g/l}$  at discharge was significantly higher than that at admission (all  $p < 0.01$ ).

Multivariate logistic regression analysis was conducted on the collected data to obtain values for the hospitalization days (OR = 1.251; 95% CI: 1.067–1.384;  $P = 0.007$ ), nasal feeding (OR = 22.623; 95% CI: 1.091–286.899;  $P = 0.013$ ), and malnutrition on admission (OR = 30.760; 95% CI: 1.064–89.797;  $P = 0.046$ ), which were statistically significant risk factors for malnutrition in RCSE. However, gender, age, mechanical ventilation, tumor, decreased consciousness level during hospitalization, tumor, pneumonia, dementia, ketogenic diet, gastrointestinal hemorrhage, diabetes, depression and dysphagia all had  $P$  values  $> 0.05$ , showing no statistical significance.

Ten patients died when discharged from the hospital, and 17 patients had MRS scores  $> 2$ . Multivariate logistic regression analysis showed that patients with malnutrition or risk of malnutrition had worse

prognosis than patients with good nutrition ( $p < 0.05$ ).

## Discussion

During hospitalization, although RCSE patients received nutritional support, various nutritional parameters still showed downward trends. The malnutrition rates were 9.59% at the time of admission and 45.21% at the time of discharge in this study. At present, there is no universally accepted definition of malnutrition, and there is no gold standard for nutrition assessment. Previous studies have found that serum albumin is the most significant indicator to reflect nutritional status and is often used to assess nutritional status, but the half-life is relatively long, approximately 14–20 days[14–15]. In addition, the use of a variety of nutrition assessment tools, such as MNA, may help to make a broad estimate of malnutrition[16]. There are many reasons for malnutrition during hospitalization, which are related to insufficient intake, gastrointestinal tract malabsorption and increased energy consumption.

In RCSE patients who fast due to consciousness disorder, gastrointestinal hemodynamics is affected due to lack of food stimulation, and gastrointestinal digestion and absorption function weaken or even disappear; thus, malnutrition occurs due to poor nutrient absorption[9, 17]. When gastrointestinal dynamics are weakened, it can lead to an increase in gastrointestinal pressure, coupled with damage to the gastrointestinal mucosal structure caused by ischemia. A large amount of bacteria and toxins in gastrointestinal tract can enter the blood, causing systemic infection and poisoning symptoms, aggravating the body's energy consumption and leading to malnutrition[17]. In this study, the level of consciousness in the malnutrition group decreased more obviously after admission; the functional status of daily activities was lower; there were more gastrointestinal complications, such as pulmonary infection, heart failure, and electrolyte disturbance; and gastrointestinal function was poor.

This study shows that malnutrition at admission, nasal feeding and hospitalization days are risk factors for malnutrition during hospitalization for patients with RCSE. Malnutrition on admission is the basis of malnutrition, which indicates that pneumonia, other infections, gastrointestinal hemorrhage, and other related conditions are more likely to occur during hospitalization, leading to decreased food consumption in patients and malnutrition. The longer the stay in the hospital is, the more likely the patients are to suffer from nosocomial infection, bedsores, gastrointestinal hemorrhage and other complications; moreover, the nutritional intake during hospitalization is worse than that after discharge. The diet accepted by nasal-feeding patients is mainly a liquid diet, such as protein powder, rice flour, etc., which carries a high risk of diarrhea.

Previous studies have shown that dysphagia is a risk factor for malnutrition after stroke, which is inconsistent with the conclusion of this study[18–23]. The reason for this difference may be that only 5 patients with RCSE caused by cerebral infarction were included in this study, and the study sample was small. More patients with cerebral infarction can be included in a follow-up study, and the sample size can be expanded and analyzed separately. Decreased consciousness levels in patients during hospitalization may also be a risk factor for malnutrition in patients with refractory epilepsy. When the

patient's consciousness level decreases, nutrition intake may decrease, and decreased intestinal peristalsis during long-term bed rest may lead to poor absorption. However, this study did not reach this conclusion, which may be because the included patients were seriously ill, and most patients had decreased levels of consciousness.

In addition to the malnutrition, nasal feeding and hospitalization days shown in this study, there may be other related risk factors. These factors include (1) concomitant consumptive diseases. In addition, (2) some patients with intractable convulsive epilepsy continued to use ketogenic diet, mainly high-fat diet, lacking protein involvement. (3) Severe complications, such as upper gastrointestinal hemorrhage, respiratory tract and urinary system infection, multiple organ failure, bedsore, and dementia increase the energy consumption of the body. (4) Depression and other mental factors can lower patients' confidence in their lives, resulting in anorexia, noncooperation with treatment and other manifestations, promoting the occurrence of malnutrition. There are also (5) Iatrogenic factors – some doctors pay one-sided attention to the role of clinical drug therapy, ignoring nutritional support therapy.

This study shows that malnutrition patients have a high incidence of poor prognosis. Patients with malnutrition may be more prone to hospital infection, gastrointestinal dysfunction and other complications, which may have occurred accidentally due to the small sample size or due to the limitations of evaluation tools. This conclusion requires further longitudinal study with larger samples.

There are still some limitations to this study. First, these data are all from West China Hospital. Although they can reflect the risk factors of malnutrition in patients with RCSE in western China to some extent, their generalizability is lower since this is a single-center study. At present, there is no universally accepted definition of malnutrition and no gold standard for nutritional assessment. Thus, these research results have certain limitations. In subsequent research, the sample size will be further expanded, and a subgroup analysis related to etiology will be conducted. Only patients over 18 years old were included in this study. These patients may have some differences with other age groups in the results of this study.

## **Conclusion**

The risk of malnutrition during hospitalization in RCSE patients is 45.21%. Malnutrition, nasal feeding and hospitalization days are risk factors for malnutrition. Malnourished patients at admission are more likely to develop malnutrition during hospitalization, and early intervention is required for these patients.

## **Declarations**

### **Ethics approval and consent to participate**

The protocol was approved by the West China hospital ethics Committee

### **Consent for publication**

I can confirm I have consent for publication

### **Availability of data and material**

I can confirm I have included a statement regarding data and material availability in the declaration section of my manuscript.

### **Competing interests**

The authors declare no conflicts of interest.

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Funding information is not applicable.

### **Authors' contributions**

Dr Zhang collects data and writes articles

Dr Chen and Dr Zhu are responsible for collation and statistics

Dr Liu reviews articles

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## **References**

1. Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, et al. A definition and classification of status epilepticus - report of the ILAE Task Force on Classification of Status Epilepticus. *Epilepsia*. 2015;56(10):1515–23
2. Glauser T, Shinnar S, Gloss D, et al. Evidence-Based Guideline: Treatment of Convulsive StatusEpilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society[J]. *Epilepsy Currents*, 2016, 16(1): 48-61.
3. Madžar D, Geyer A, Knappe RU, et al. Association of seizure duration and outcome in refractory status epilepticus. *J Neurol*. 2016;263:485–91.
4. Hocker S, Britton JW, Mandrekar JN, et al. Predictors of outcome in refractory status epilepticus. *JAMA Neurol*. 2013;70:72–7.
5. Rosenow F, Hamer HM, Knake S. The epidemiology of convulsive and nonconvulsive status epilepticus. *Epilepsia*. 2007;48:82–4.6.

6. Leitinger M, Höller Y, Kalss G, Rohracher A, Novak HF, Höfler J. Epidemiology-based mortality scale in status epilepticus (EMSE). *Neurocrit Care* 2015;22:273–82.7.
7. Koubeissi M, Alsheklee A. In-hospital mortality of generalized convulsive status epilepticus. *Neurology*. 2007;69:886–93.
8. Lai A, Outin H, Jabot J, et al. Functional outcome of prolonged refractory status epilepticus. *Crit Care*. 2015;19:199.
9. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr* .2017;36(1):49-64.
10. White JV, Guenter P, Jensen G, Malone A, Schofield M. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *J Acad Nutr Diet*.2012;112(5):730-8.
11. Suter PM. Alcohol, nutrition and health maintenance: selected aspects. *Proc Nutr Soc* .2004;63(1):81-8.
12. Lipkin EW, Bell S. Assessment of nutritional status: the clinician's perspective. *J Clin Lab Med* 1993;13: 329.
13. MacIntosh C, Morley JE, Chapman IM. The anorexia of aging[J]. *Nutrition*, 2000, 16:983-995.
14. Elia M, Stroud M. Nutrition in acute care[J]. *Clin Med*, 2004, 4:405-407.
15. Donini LM, Savina C, Cannella C. Eating habits and appetite control in the elderly: the anorexia of aging[J].*Int Psychogeriatr*, 2003, 15:73-87.
16. Guigoz Y, Vellas BJ, Garry PJ. Mini Nutritional Assessment: a practical assessment tool for grading the nutritional state of elderly patients. *J Facts Res Gerontol* 1994;4( 2) : 15-59.
17. Donini LM, De Bernardini L, De Felice M, et al. Effect of nutritional status on clinical outcome in a population of geriatric rehabilitation patients. *J Aging Clin Exp Res* 2004; 16( 2) : 132-138.
18. Wang W, Jiang B, Sun H, Ru X, Sun D, Wang L, et al. Prevalence, incidence, and mortality of stroke in China: results from a nationwide population-based survey of 480,687 adults. *Circulation*. 2017;135(8):759-71.
19. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990-2010: findings from the global burden of disease study 2010. *Lancet (London, England)*.2014;383(9913):245-54.
20. Gomes F, Emery PW, Weekes CE. Risk of malnutrition is an independent predictor of mortality, length of hospital stay, and hospitalization costs in stroke patients. [J] *Stroke Cerebrovasc Dis Off J Nat Stroke Assoc* .2016;25(4):799-806.
21. Davalos A, Ricart W, Gonzalez-Huix F, Soler S, Marrugat J, Molins A, et al. Effect of malnutrition after acute stroke on clinical outcome. *Stroke* .1996;27(6):1028-32.
22. Zhao YY, Zeng W. Nutritional status and influencing factors of malnutrition in elderly patients with stroke. *Chin J Gerontol*. 2016;36:2372-3.

23. Aquilani, P. Sessarego, P. Iadarola, A. Barbieri, and F. Boschi, Nutrition for brain recovery after ischemic stroke: an added value to rehabilitation. *Nutrition in Clinical Practice*. 2011, 26(3): 339–345.

## Tables

Table 1: Demographic and clinical data of patients included

	Total (n=73)	Malnutrition (n=33/45.2%)	P value
Gender (male%)	44 (60.3%)	16 (21.9%)	0.000
Age (years) (range)	40±20	39±21	0.000
Hospital stays (day)	44±23	82±49	0.000
Cost (thousand dollar)	149611±314605	303997±420872	0.000
BMI (kg / m <sup>2</sup> )	55±30	50±25	0.000
Albumin (g / L)	41±10	30±7	0.000
Pathogen			
CNS-infection acute	30	15	
Head trauma	3	1	
Brain tumor	7	4	
CNS-anomalies	7	2	
cerebrovascular disease	5	2	
Anoxia	4	1	
Metabolic sodium balance and metabolic disorder	6	4	
Drug reduction/withdrawal (poor compliance)	11	4	
Malnutrition on admission	7	5	
Diabetes mellitus	11	5	
Tube feeding	31	28	
Reduced level of consciousness	25	23	
Depressed mood	8	4	
Pneumonia and infection	48	30	
Tumor	6	3	
Gastrointestinal bleeding	15	11	
Dementia	3	1	
Ketone diet	1	1	
Dysphagia	4	4	
Need for tracheal intubation	27	26	

Table 2 Nutritional Status of Stroke Patients at Different Time Points of Admission

	Admission	7day	14day	Discharge
Weight loss is greater than 6% of the body weight at admission	0	2	10	15
BMI $\geq 18.5$ kg /m <sup>2</sup>	4	8	14	18
Albumin $\geq 35$ g / L	3	9	13	19
MNA $\geq 17$	2	9	18	33

Table 3 Risk factors for malnutrition in patients with refractory status epilepticus

	Total $\geq 73$	P-value	OR	95%CI
Male	44 $\geq 60.3\%$	0.529	0.189	0.002-17.306
Age	40 $\pm 20$	0.356	1.058	0.938-1.098
Hospital stays $\geq$ day $\geq$	44 $\pm 23$	0.007	1.251	1.067-1.384
Malnutrition on admission	7	0.042	30.760	1.064-89.797
Diabetes mellitus	11	0.734	2.314	0.018-234.998
Tube feeding	31	0.013	22.623	1.091-286.899
Reduced level of consciousness	25	0.137	0.048	0.001-2.645
Depressed mood	8	0.695	0.504	0.017-15.394
Pneumonia and infection	48	0.629	3.180	0.111-7.218
Tumor	6	0.664	0.472	0.015-14.865
Gastrointestinal bleeding	15	0.750	2.334	0.013-433.271
Dysphagia	4	0.079	29.133	0.680-456.372
Need for tracheal intubation	27	0.320	22.336	0.025-197.623

