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Multivariate Logistic Regression Analysis of Risk Factors for Subacute Delirium Syndrome in ICU Patients

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Abstract: *Objective*: This study aimed to identify risk factors for subsyndromal delirium (SSD) in adult intensive care unit (ICU) patients using a multivariate logistic regression model. *Methods*: A total of 252 ICU patients admitted to a Grade A tertiary hospital between January 2024 and December 2025 were included in the study. General characteristics, clinical conditions, treatments and laboratory test results were compared between 174 patients who developed SSD and 78 who did not. Univariate risk factors for SSD were identified, and multivariate logistic regression analysis was performed to determine the independent risk factors for SSD. *Results*: Multivariate logistic regression analysis revealed that patient age (OR = 1.465), Acute Physiology and Chronic Health Evaluation II (APACHE II) score (OR = 1.677), Critical Care Pain Observation Tool (CPOT) score (OR = 1.899), physical restraint (OR = 3.485), sepsis (OR = 2.452) and duration of mechanical ventilation (OR = 1.635) were identified as independent risk factors for SSD in ICU patients. *Conclusion*: Elderly ICU patients are at higher risk of developing sub-delirium syndrome; early screening and timely medical intervention can reduce the risk of SSD and improve patient prognosis.

Keywords: Subsyndromal delirium (SSD); Intensive care unit (ICU); Risk factors; Multivariate logistic regression

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1. Introduction

Subacute delirium syndrome (SSD) is an acute state of brain dysfunction that does not fully meet the diagnostic criteria for delirium but is characterized by impairments in attention, cognition, mood, or sleep. Recent studies indicate that the incidence of SSD in intensive care unit (ICU) patients ranges from 17% to 86%, far exceeding that of typical delirium; however, due to its insidious symptoms and rapid progression, it poses significant challenges for clinical identification and intervention [1]. SSD represents a critical precursor to delirium; its occurrence and progression are closely associated with adverse outcomes such as long-term cognitive impairment, mechanical ventilation and prolonged hospital stays, placing a heavy burden on

patients' families and the healthcare system. Currently, both domestic and international research on SSD in ICU patients has largely focused on descriptive surveys, with a relative lack of in-depth analysis of specific risk factors, which directly limits the early identification of high-risk patients and targeted prevention [2] .Therefore, this study aims to conduct a prospective observational study to systematically analyze the risk factors associated with SSD in ICU patients and construct a multivariate logistic regression model. The objective is to provide evidence-based support for the early clinical screening of high-risk individuals and the implementation of targeted interventions, thereby improving patient outcomes.

2. Materials and methods

2.1. General information

A prospective observational study design was employed. A total of 252 patients admitted to the general ICU of a Grade A tertiary hospital between 1 January 2024 and 31 December 2025 were consecutively enrolled. Participants were categorized into a delirium group (n = 174) and a non-delirium group (n = 78) based on the occurrence of SSD during their ICU stay.

2.1.1. Inclusion criteria

(1) Age ≥ 18 years;
(2) ICU stay ≥ 24 hours;
(3) Informed consent from the patient or their legal representative.

2.1.2. Exclusion criteria

(1) History of neurological diseases with a confirmed diagnosis, such as dementia, Parkinson's disease, sequelae of stroke, or intracranial tumors;
(2) History of psychiatric or psychological disorders prior to admission;
(3) Severe visual, hearing, or speech impairments affecting cognitive assessment;
(4) Patients in a deep coma upon admission to the ICU or those expected to require deep sedation throughout their ICU stay.

2.2. Methods

2.2.1. Collection of general and clinical data

The following data were collected by reviewing electronic medical records:

(1) General information

Gender, age, educational attainment, marital status.

(2) Disease and treatment-related factors

Acute Physiology and Chronic Health Evaluation II (APACHE II) score within 24 hours of admission; Critical Care Pain Observation Tool (CPOT) score; diagnosis of sepsis (referring to the Sepsis-3.0 criteria); use of analgesics/sedatives during hospitalisation, use of physical restraints, and administration of blood products; total number of indwelling catheters; total length of stay; total duration of mechanical ventilation.

(3) Laboratory parameters

Relevant parameters collected within 24 hours of ICU admission, including serum albumin (hypoalbuminaemia: < 30 g/L), arterial blood carbon dioxide partial pressure ($PaCO_2$, hypercapnia: > 45

mmHg), and C-reactive protein (CRP, elevated > 10 mg/L) [3].

2.2.2. Richmond agitation-sedation scale (RASS)

Assesses the patient's level of consciousness and depth of sedation; the score ranges from -5 (unresponsive) to +4 (agitated), with assessments conducted twice daily. Scores of -1 to -5 indicate varying degrees of sedation; a score of 0 indicates the patient is alert and calm; scores of 1 to 4 indicate agitation and anxiety [4].

2.2.3. The ICU confusion assessment method (CAM-ICU)

The ICU Confusion Assessment Method (CAM-ICU) is widely recognized as the "gold standard" for diagnosing delirium in ICU patients [5]. This scale comprises four criteria:

(1) Acute change or fluctuation in level of consciousness;
(2) Disorientation;
(3) Change in level of consciousness as determined by the RASS;
(4) Disorganized thinking.

A diagnosis of delirium is made when the patient meets criteria (1) + (2) + (3) or (1) + (2) + (4) simultaneously. When a patient exhibits only one or several of the above characteristics but does not fully meet the diagnostic criteria for delirium, the condition is classified as SSD.

2.3. Statistical analysis

Data analysis was performed using SPSS 26.0 and R 4.3.1 software. Quantitative data conforming to a normal distribution are presented as mean ± standard deviation ($\overline{x} \pm s$), with comparisons between groups performed using the independent samples *t*-test; categorical data are presented as frequency (percentage) [n(%)], with comparisons between groups performed using the chi-square test. Variables with $p < 0.1$ in the univariate analysis were included in a multivariate binary logistic regression model (stepwise method, LR) to analyze independent risk factors for the occurrence of SSD, and odds ratios (OR) and their 95% confidence intervals (CI) were calculated. All statistical tests were two-sided; $p < 0.05$ was considered statistically significant.

3. Results

3.1. Univariate analysis of SSD occurrence in ICU patients

The results of the univariate analysis showed that there were statistically significant differences between the SSD group and the non-SSD group in terms of age, APACHE II score, CPOT score, length of hospital stay, use of sedative-analgesic drugs, physical restraint, sepsis, use of blood products, CRP levels, and duration of mechanical ventilation (all $p < 0.05$). There were no statistically significant differences between the two groups in terms of gender, educational level, marital status, hypoproteinaemia, or hypercapnia ($PaCO_2$) ($p > 0.05$); see **Table 1**.

Table 1. Univariate analysis of subdelirium syndrome in ICU patients

Item	Subdelirium group(n = 174)	Non-delirium group (n = 78)	t/χ^2 value	*p*-value
Age ($\overline{x} \pm s$, years)	60.12 ± 2.14	59.45 ± 2.17	2.288	0.023

Item		Subdelirium group(n = 174)	Non-delirium group (n = 78)	t/χ^2 value	*p*-value
Gender [n(%)]	Male	92	42	0.021	0.886
	Female	82	36		
Educational attainment [n(%)]	Primary school and below	97	35	5.052	0.080
	Lower secondary or upper secondary	52	23		
	College or above	25	20		
Marital status [n(%)]	Married	150	68	0.062	0.970
	Unmarried	9	4		
	Divorced or widowed	15	6		
APACHE II score ($\overline{x}$ ± s, points)		9.48 ± 1.36	10.12 ± 1.26	3.531	< 0.001
CPOT score ($\overline{x}$ ± s, points)		1.25 ± 0.34	1.04 ± 0.26	4.854	< 0.001
Length of stay ($\overline{x}$ ± s, days)		9.55±2.05	6.52 ± 2.11	10.749	< 0.001
Use of sedative-analgesic drugs [n(%)]	Yes	105	21	24.064	< 0.001
	No	69	57		
Constraint [n(%)]	Yes	119	15	52.274	< 0.001
	No	55	63		
Sepsis [n(%)]	Yes	35	4	9.247	0.002
	No	4	74		
Use of blood products [n(%)]	Yes	78	24	4.418	0.036
	No	96	54		
Hypoproteinaemia [n(%)]	Yes	108	40	2.586	0.108
	No	66	38		
Elevated $PaCO_2$[n (%)]	Yes	24	10	0.044	0.835
	No	150	68		
CRP [n (%)]	Normal	82	57	14.664	< 0.001
	Elevated	92	21		
Duration of mechanical ventilation ($\overline{x}$ ± s, h)		209.15 ± 7.89	198.36 ± 8.52	9.789	< 0.001

3.2. Logistic regression analysis of SSD incidence in ICU patients

The results of the multivariate logistic regression analysis showed that age, APACHE II score, CPOT score, physical restraint, sepsis and duration of mechanical ventilation were independent risk factors for SSD in ICU patients (all $p < 0.05$). Among these, physical restraint posed the highest risk (OR = 3.485), followed by sepsis (OR = 2.452) and pain (CPOT score, OR = 1.899), as shown in **Table 2**.

Table 2. Logistic regression analysis of SSD in ICU patients

Variable	Value	β	SE	Wald χ^2	*p*-value	OR	95% CI
Age (years)	Original value	0.382	0.167	5.241	0.022	1.465	1.058–2.028
APACHE II score (points)	Original value	0.517	0.189	7.396	0.007	1.677	1.152–2.441
CPOT score (points)	Original value	0.642	0.213	9.185	0.002	1.899	1.268–2.843
Length of stay (days)	Original value	0.279	0.158	3.098	0.078	1.321	0.972–1.794
Use of sedative-analgesic drugs	No = 0, Yes = 1	0.315	0.192	2.716	0.099	1.370	0.935–2.007
Constraint	No = 0, Yes = 1	1.248	0.285	19.152	< 0.001	3.485	2.079–5.832

Sepsis	No = 0, Yes = 1	0.897	0.321	7.864	0.005	2.452	1.318–4.561
Use of blood products	No = 0, Yes = 1	0.294	0.176	2.773	0.096	1.342	0.950–1.899
CRP	Normal = 0, elevated = 1	0.368	0.201	3.339	0.068	1.445	0.973–2.145
Duration of mechanical ventilation (h)	Original value	0.492	0.174	7.963	0.005	1.635	1.149–2.328

4. Discussion

ICU patients often present with complex conditions such as multiple organ dysfunction and severe infections, and frequently require invasive treatments including mechanical ventilation, analgesia and sedation, and the administration of vasoactive drugs; all such procedures and medications may interfere with the body's normal physiological state. Furthermore, given the rapid progression of ICU patients' conditions and significant individual variability, the symptoms of subacute delirium syndrome are subtle. In the early stages, they manifest only as mild inattention and sleep disturbances, which are easily masked by symptoms of severe underlying diseases. This leads to delayed clinical recognition, missed opportunities for intervention, and an increased risk of poor outcomes [6]. Subacute delirium syndrome (SSD) is an acute cerebral dysfunction lying between normal consciousness and delirium; although it does not meet the diagnostic criteria for delirium, it involves mild impairment in attention, cognition, mood and sleep, and represents an important precursor to the development of delirium [7]. Therefore, identifying the risk factors for SSD in ICU patients can, on the one hand, assist clinical staff in accurately identifying high-risk groups, establishing early screening mechanisms, and implementing targeted prevention; on the other hand, it enables the development of individualized interventions to reduce the incidence of SSD, prevent its progression to delirium, and improve the quality of care for critically ill patients.

Multivariate logistic regression analysis in this study revealed that age, APACHE II score, CPOT score, physical restraint, sepsis, and duration of mechanical ventilation are independent risk factors for SSD in ICU patients. Based on clinical practice, the reasons are analyzed as follows:

(1) As people age, the brain parenchyma undergoes degenerative changes, cerebral blood supply becomes inadequate, and the regulatory functions of the central nervous system decline. This leads to a significant reduction in tolerance to external stimuli such as pain, infection and medication. Furthermore, the presence of multiple underlying conditions often makes brain function more susceptible to damage, thereby increasing the risk of SSD.

(2) The APACHE II score reflects the severity of a patient's acute physiological injury and chronic health status. A higher score indicates a more critical condition and a more intense physiological stress response; the massive release of stress hormones can interfere with central nervous system function. Furthermore, critically ill patients often suffer from metabolic disorders and hypoxia, which further exacerbate brain damage and induce SSD.

(3) A high CPOT score indicates a more severe level of pain. Persistent pain stimuli activate the body's stress response, impairing sleep quality and leading to poor concentration and emotional disturbances. Furthermore, pain necessitates increased doses of sedative and analgesic medications, which indirectly interfere with brain function and heighten the risk of SSD.

(4) ICU patients may require physical restraints due to agitation or catheter maintenance; these restrict limb movement, impair positional changes and blood circulation, and exacerbate cognitive impairment,

leading to negative emotions such as anxiety and fear, thereby inducing SSD.

(5) In patients with sepsis, the systemic inflammatory response leads to the massive release of inflammatory mediators into the bloodstream. These cross the blood-brain barrier and damage brain tissue, causing dysfunction of the central nervous system. Furthermore, sepsis is often accompanied by fever, hypoxia and metabolic acidosis, which further exacerbate brain damage and increase the risk of SSD.

(6) Prolonged mechanical ventilation can cause airway discomfort and communication difficulties in patients, and may even lead to complications such as pulmonary infection and hypoxia. This continuously stimulates the central nervous system, disrupts the homeostasis of brain function, and induces SSD [8].

5. Conclusion

In summary, the occurrence of SSD in ICU patients is influenced by multiple factors. Clinically, targeted intervention measures should be developed to address the aforementioned risk factors, with early screening of high-risk groups and timely intervention to reduce the incidence of SSD and improve patient prognosis.

Disclosure statement

The authors declare no conflict of interest.

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