

Delirium in a Medical Intensive Care Unit: Prevalence, Risk Factors and Outcomes

Chairat Permpikul, M.D., Wasin Jirisan, M.D., Surat Tongyoo, M.D., Varalak Srinonprasert, M.D.

Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: Delirium is a common problem in critical care. Its prevalence in the unit varies, depending upon the severity of the illness and the diagnostic methods. Currently, the CAM-ICU is a diagnostic tool with good diagnostic accuracy. Our study aimed to determine the prevalence, associated factors, and outcomes of delirium in our unit by using the CAM-ICU.

Methods: Our prospective cohort study included all patients admitted to the hospital's medical ICU from August to December, 2013. Patients with psychosis and/or in a coma (RAAS<-3) were excluded. We assessed delirium by using the CAM-ICU within the first 24 hours of admission and then serially, every 48 hours until discharge. Factors associated with this condition and patients' outcomes were also explored.

Results: A total of 74 patients were included. Of these, 43% were male, 40% had sepsis, and 81% were mechanically ventilated. Twenty-eight patients (38%) had delirium upon admission. The delirium patients were older and had a higher percentage of dementia. Univariate analysis revealed that dementia, anemia, acute metabolic acidosis, and the use of mechanical ventilation were associated with the occurrence of delirium, and, for age > 70 years, anemia and metabolic acidosis remained significant on multivariate analysis. Delirium was significantly associated with prolonged hospitalization (>30 days), with OR = 4.84 (p=0.009), and with increased mortality, with OR = 25.0 (p=0.001).

Conclusion: This study confirmed that delirium was common in the medical ICU and was associated with poor outcomes. Importantly, associated factors with delirium in our study appeared to be modifiable. Further study on early management and prevention of those risk factors is crucial.

Keywords: Delirium; critically ill patients; CAM-ICU (Siriraj Med J 2021; 73: 155-160)

INTRODUCTION

Delirium is a syndrome of acute brain dysfunction defined as a disturbance in attention and awareness from the baseline. Changes in cognition not better accounted for by a preexisting, established, or evolving dementia occurs in this setting. The condition develops over a short period and fluctuates in severity during the course of a day.¹ Many terms have been used to describe this condition: intensive care unit (ICU) psychosis, postoperative delirium, and ICU syndrome.^{2,3} Delirium should be differentiated

from dementia, major depression, and psychogenic illness. Studies have revealed that ICU delirium was associated with poor clinical outcomes, such as a prolonged length of hospital stay, functional and cognitive decline, and increases in mortality and morbidity.⁴⁻⁶ A systemic review in medical wards demonstrated that delirium was associated with increased mortality at discharge and at 12 months, as well as with an increased length of hospital stay. Persistent symptoms of delirium might be found at discharge and at 6 to 12 months thereafter.⁷

Corresponding author: Chairat Permpikul

E-mail: chairat.per@mahidol.ac.th

ORCID ID: <http://orcid.org/0000-0001-5491-6987>

Received 1 October 2020 Revised 25 November 2020 Accepted 4 February 2021

<http://dx.doi.org/10.33192/Smj.2021.20>

The prevalence of delirium has varied among the studies. In the hospital setting, it has ranged from 6-56%⁸; in post-operative surgical ICUs, it has ranged from 15-53%; and in medical-surgical ICUs, from 20-80%.⁹⁻¹¹ This has depended on the severity of illness and the diagnostic method.¹² The prevalence of delirium in elderly patients in our institution was 48%. Those who had this condition had a longer length of stay and an increased in-hospital mortality¹³ than others.

There are certain difficulties in the diagnosis of ICU delirium, especially regarding mechanically ventilated patients. As a result, many scoring systems have been developed. Examples include the Confusion Assessment Method for the ICU (CAM-ICU); the Nursing Delirium Screening Scale (Nu-DESC); and the Delirium Detection Score (DDS). Among these, the CAM-ICU has had the highest validity,¹⁴ with sensitivities of 95-100%, specificities of 89-93%, and a high inter-rater reliability.¹⁵ The CAM-ICU has been translated into Thai.¹⁶ It has been back-translated, reviewed, and validated.¹⁷ The results have revealed a sensitivity of 92.33%, a specificity of 94.7%, and high inter-rater reliability (Cohen's kappa = 0.82; p-value < 0.001). Our study primarily aimed to determine the prevalence of delirium in our unit by using the Thai CAM-ICU. The secondary objectives were to assess associating factors, including the outcomes of this condition.

MATERIALS AND METHODS

Study design

This prospective cohort study included all patients who were admitted to the Medical ICUs at Siriraj Hospital in Bangkok from August to December, 2013. Exclusion criteria included psychosis, coma (The Richmond Agitation and Sedation Scale, RASS < -3), aphasia and being unable to Thai language communication. Our unit is a 16 beds facility a tertiary care unit with nurse to patient ratio 1:1 during day time and 1:2 at night. During the study period, there was no standard protocol for sedatives and analgesic agents usage available in our ICU. The decision to prescribe sedatives and analgesic agents were depended on the attending physician judgment.

Delirium Assessment

All patients were screened for delirium using the CAM-ICU (Thai version). Delirium assessments were undertaken within the first 24 hours of admission and serially every 48 hours until discharge or death. One of the authors (W.J.) was the assessor of delirium.

The recorded patient characteristics including age, sex, alcohol consumption, history of dementia, history of

delirium, and basic activities of daily living (ADL). The APACHE-II illness score and the Modified Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)¹⁷ were assessed. The presence of infection, anemia, acute metabolic acidosis, dysnatremia, and therapeutic details such as mechanical ventilation and sedation medication were noted. Anemia was diagnosed if the patient's blood test during ICU admission showed hematocrit less than 30%. Acute metabolic acidosis was documented if there was a result of arterial blood gas analysis, performed during ICU admission showed blood pH less than 7.25 with partial carbondioxide pressure lower than 40 mmHg. Dysnatremia was defined as having serum sodium lower than 135 mmol/l or more than 145 mmol/l during ICU admission. Clinical-outcomes data such as the hospital length of stay and the hospital mortality rate were explored between the delirium and non-delirium groups.

Statistical analysis

All data analyses were performed using SPSS Statistics version 18 (SPSS, Inc., Chicago, IL, USA). Continuous data were checked for normal distribution by using Shapiro-Wilk test. All continuous data with normal distribution were presented using mean and standard deviation. The continuous variables with non-normal distribution were presented with median and interquartile range. To comparison between delirium and non-delirium group, the independent *t*-test was used to compare the continuous variables with normal distribution, and Mann-Whitney U test was used for non-normal data distributions. Categorical data are presented in percentages indicating the prevalence of the factor in either the delirium or the non-delirium group. Pearson Chi-squared or Fisher exact test was used, when suitable, to compare the categorical data between groups. Univariate analysis was performed to identified independent predictive factors associated with delirium during ICU admission. All the variables with a P-value less than 0.1 in univariate analysis were included in multivariate analysis. The logistic regression multivariate analyses were used to calculate the differences between the delirium and non-delirium groups. In the multivariate model, P-values less than 0.05 were considered statistically significant.

Ethical statement

The study protocol was reviewed and approved by the Institutional Review Board of Siriraj Hospital, Mahidol University (Si 707/2013).

RESULTS

A total of 88 patients underwent initial screening. Of these, 74 fulfilled the entry criteria and were enrolled in the study. Among 14 patients who were excluded, nine had RASS < -3 (n=9); two had a diagnosis of psychosis; and three were under sedative medications. By using the Thai version of CAM-ICU, a diagnosis of delirium was made for 28 patients (38%). Table 1 presents the general information regarding the patients who developed delirium and those who did not. Patients with delirium were older (67.8 ± 15.7 vs. 53.6 ± 19.2 year, $p = 0.002$). However, patients' basic ADL, ICQCODE, and APACHE II scores were similar. There was no difference among underlying diseases, except that more dementia patients were found in the delirium group [4 out of 28 patients (14.3%) vs. 1 in 46 patients (2.2%), $p = 0.04$]. The reasons for ICU admission included sepsis/septic shock (35 patients, 47.2%), respiratory failure (27 patients, 36.5%), acute myocardial infarction (five patients, 6.7%), and hemorrhagic shock (three patients, 4%). Also, there was no difference in the causes of admission among the groups. The sedative and analgesic medications were used in small proportion of our patients, which was no significant different between groups. (Table 2)

Physiologic alteration and the treatment and outcomes of patients with and without delirium are shown in Table 2. There was a higher proportion of anemia and acute metabolic acidosis in the delirium group [anemia 26 (92.9%) vs. 31 (67.4%), $p = 0.01$ and acute metabolic acidosis 20 (71.4%) vs. 16 (34.8%), $p = 0.002$]. As for ICU treatment, a higher proportion of delirium patients underwent mechanical ventilation [26 (92.9%) vs. 34 (73.9%), $p = 0.04$], while the use of vasopressors and renal-replacement therapy were similar. Eleven patients in this study died and 10 had delirium. Thus, hospital mortality was much higher in the delirium group [10 (35.7%) vs. 1 (2.2%) patients, $p < 0.001$]. The duration of admission tended to be longer in the delirium group, but did not reach a significant limit [28.1 ± 17.7 vs. 21.2 ± 13.5 days, $p = 0.06$].

Factors associated with delirium were examined, as is shown in Table 3. Univariate analysis revealed that dementia, anemia, acute metabolic acidosis, and mechanical ventilatory support were associated with the occurrence of delirium. After being adjusted in multivariate analysis, we found that, for age > 70 years, anemia and acute metabolic acidosis remained significant, with odd ratios of 3.53 (1.01-12.36), $p = 0.04$; 8.24 (1.16-58.35), $p = 0.04$; and 5.90 (1.71-20.37), $p = 0.005$, respectively.

DISCUSSION

In sum, using the Thai version of CAM-ICU, we found that a substantial proportion of our medical ICU patients had delirium. This condition was significantly associated with age > 70 years, anemia, and acidosis. Delirium resulted in higher mortality and tended to prolong one's hospital stay.

The prevalence of delirium in our study paralleled what others have concluded. First, the "Delirium Epidemiology in Critical Care (DECCA)" study, a one-day point-prevalence study in 104 intensive care units across Latin America, along with two centers in Spain and the U.S.,²⁰ produced interesting results. The majority of patients had a medical condition. By using the CAM-ICU, those researchers identified delirium in 32% of the patients. They also noted a threefold increase in ICU mortality and a greater-than-twofold increase in the median ICU length of stay among delirium patients. Further, Ely et al., reported a high delirium prevalence in medical ICUs. With reference to the DSM-IV criteria, 39 (81.3%) of 48 patients developed delirium, and of these, 29 (60.4%) had delirium while still in the ICU. The researchers also found that the condition was strongly associated with prolonged hospital stays. Recently, a report from India²¹ was based on 280 medical ICU patients. By using the CAM-ICU, researchers identified a delirium prevalence of 31.4%. Of these, approximately 56% had the hypoactive type, while 34% and 10% were of the hyperactive and mixed type, respectively. Like others, patients with delirium had a longer hospital stay and a higher one-month post-discharge mortality. Report from the surgical ICU of our institution²² revealed a delirium incidence of 24%. Age, diabetes mellitus, severity of disease, postoperative use of benzodiazepines and mechanical ventilation were independent risk factors. Our results here reveal the same prevalence. Interestingly, approximately one-third (35.7%) of delirium patients died, and almost all (90.9%) of the patients who died had delirium.

Although the pathophysiology of delirium is not completely understood, evidence suggests that imbalanced neurotransmitter activity such as decreased acetylcholine, increased dopaminergic activity, and a deranged serotonin level play important roles. Impaired oxidative metabolism such as shock, sepsis, and decreased cerebral perfusion are common leading factors. This is a prevailing explanation for the significant association of anemia and acute metabolic acidosis in this report. These conditions, together with advanced age (>70 years), were comparable to what other studies have shown. However, other risks identified only in univariate analysis in our study were significant

TABLE 1. Patients' baseline characters.

Clinical Characters	Delirium (n=28)	Non-Delirium (n=46)	P
Age, years	67.8+15.7	53.6+19.2	0.002
Age >70 years, n (%)	14 (50.0)	13 (28.3)	0.06
Male gender, n (%)	17 (60.7)	22 (47.8)	0.28
APACHE II score [†]	19.2+8.0	16.5+7.3	0.14
APACHE II score >20	14 (50.0)	13 (28.3)	0.06
Underlying conditions, n (%)			
Diabetes mellitus	10 (35.7)	12 (26.1)	0.38
Hypertension	9 (32.1)	13 (28.3)	0.72
Chronic kidney disease	9 (32.1)	7 (15.2)	0.09
Chronic ischemic heart disease	4 (14.3)	6 (13.0)	0.88
Chronic lung disease	3 (10.7)	6 (13.0)	0.77
Atrial fibrillation	3 (10.7)	5 (10.9)	0.98
Cerebrovascular disease	4 (14.3)	3 (6.5)	0.27
Cirrhosis	2 (7.1)	4 (8.7)	0.81
Dementia	4 (14.3)	1 (2.2)	0.04
Reasons for ICU admission, n (%)			
Septic shock	15 (53.6)	20 (43.5)	0.4
Acute respiratory failure	10 (35.7)	17 (37.0)	0.91
Acute myocardial infarction	2 (7.1)	3 (6.5)	0.66
Hemorrhagic shock	2 (7.1)	1 (2.2)	0.29

Data are presented as mean+standard deviation or number (percentage per group)

[†]The APACHE II (Acute Physiology and Chronic Health Evaluation) score, a severity-determining score, ranges from 0 to 71. Higher scores indicate a more severe disease.

TABLE 2. Patients' clinical events, treatments, and outcomes.

Clinical characters	Delirium (n=28)	Non-Delirium (n=46)	P
Acute physiologic conditions, n (%)			
Anemia	26 (92.9)	31 (67.4)	0.01
Dysnatremia	23 (82.1)	28 (60.9)	0.06
Acute metabolic acidosis	20 (28.6)	16 (34.8)	0.002
Sedative and analgesic agents, n (%)			
Benzodiazepine plus opioid analgesia	3 (10.7)	9 (19.6)	0.36
Opioid analgesia alone	2 (7.1)	8 (17.4)	0.30
Benzodiazepine alone	2 (7.1)	6 (13.0)	0.48
Treatment during ICU admission, n (%)			
Mechanical ventilation	26 (92.9)	34 (73.9)	0.04
Receiving vasopressors	19 (67.9)	24 (52.2)	0.19
Require renal- replacement therapy	4 (14.3)	5 (10.9)	0.66
Duration of admission [†] , days	28.1+17.7	21.2+13.5	0.06
Duration of admission >30 days, n (%)	11 (39.3)	10 (21.7)	0.10
Hospital mortality, n (%)	10 (35.7)	1 (2.2)	<0.001
RR 7.86 (95%CI: 1.21-51.25)			

[†] Duration of admission was overall hospital admission day

TABLE 3. Predictive factors associated with new-onset delirium during ICU admission.

Clinical characters	Univariate analysis			Multivariate analysis		
	Relative risk	95% CI	P	Relative risk	95% CI	P
Age >70 years	1.46	0.95-2.25	0.06	3.53	1.01-12.36	0.04
Chronic kidney disease	1.54	0.86-2.76	0.09	2.39	0.58-9.82	0.23
Dementia	2.30	1.33-3.97	0.04	3.86	0.31-48.01	0.99
APACHE II score >20	1.46	0.95-2.25	0.06	3.04	0.93-9.97	0.07
Anemia	3.88	1.02-14.69	0.01	8.24	1.16-58.35	0.04
Abnormal electrolyte	2.08	0.90-4.77	0.06	1.14	0.25-5.27	0.29
Acute metabolic acidosis	2.64	1.34-5.22	0.002	5.90	1.71-20.37	0.005
Mechanical ventilation	3.03	0.81-11.30	0.04	4.64	0.67-32.05	0.12

in others.²¹ Moreover, we did not find any link between delirium and the uses of certain medications, such as anticholinergics, benzodiazepines, and opiates, which was significant in the surgical ICU.²² The low number of patients and the infrequent use of sedation in our unit are possible explanatory factors.

Knowing the mortality risk of delirium and its associated factors, we can take measures to prevent this condition. Rapid restoration of shock will mitigate the perfusion deficit, acidosis, and inflammation.²³⁻²⁵ Timely source control of sepsis can lead to successful resuscitation. Thoughtful uses of organ support, namely mechanical ventilation and renal-replacement therapy, can minimize physiologic derangement stemming from life-saving measures.

Apart from the above findings, our study and earlier works support the use of the CAM - ICU as a bedside diagnostic tool for delirium. The simplicity and repeatability of the test enable clinicians to perform it routinely. Intensivists can conduct the test during daily rounds. Early recognition of acute brain dysfunction enables early intervention.

Our study had some limitations. First, the number of patients was small, as compared to other studies. The relatively small sample sized could resulted in inadequate power to detect the actual predictive factor, as well as, the wide range of 95% confidence interval for each predictive factor. A larger number might allow us to identify more

predictive factors associated with delirium. Moreover, the study period was short, both in terms of the recruitment period and the duration of the follow-up. A longer study period should enable us to recruit more patients and detect both physical and cognitive impairments which have been found in other studies.^{26,27} Finally, this study enrolled patients during August to December 2013. The progression of medical technology and treatment strategy now a day might affect to the nature of delirium among critically ill patients. Physician who decide to apply the results of this study to their clinical practice should carefully evaluate the context of this study and compare it with their own situation.

In conclusion, our report demonstrates that, by using the Thai version of the CAM-ICU, it was determined that approximately one-third of medical ICU patients had delirium. Patients with this condition had a high mortality and a prolonged hospital stay. In addition, some factors associated with this condition were identified. Aggressive resuscitation of critically ill patients in order to avoid these risks, such as early goal-directed resuscitation and optimum metabolic support, are essential to success.

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. 5th ed. Washington, DC: American Psychiatric Association; 2013.
2. McGuire BE, Basten CJ, Ryan CJ, Gallagher J. Intensive care unit syndrome: a dangerous misnomer. *Arch Intern Med* 2000;160: 906-9.

3. Justic M. Does "ICU psychosis" really exist? *Crit Care Nurse* 2000;20:28-37.
4. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. *Intensive Care Med* 2001; 27:859-64.
5. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE Jr, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 2004;291: 1753-62.
6. Jackson JC, Gordon SM, Hart RP, Hopkins RO, Ely EW. The association between delirium and cognitive decline: a review of the empirical literature. *Neuropsychol Rev* 2004;14:87-98.
7. Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. *Age Ageing* 2006;35:350-64.
8. Inouye SK. Delirium in hospitalized older patients. *Clin Geriatr Med* 1998;14:745-64.
9. Pisani MA, McNicoll L, Inouye SK. Cognitive impairment in the intensive care unit. *Clin Chest Med* 2003;24:727-37.
10. Dubois MJ, Bergeron N, Dumont M, Dial S, Skrobik Y. Delirium in an intensive care unit: a study of risk factors. *Intensive Care Med* 2001;27:1297-304
11. Ely EW, Stephens RK, Jackson JC, Thomason JW, Truman B, Gordon S, et al. Current opinions regarding the importance, diagnosis, and management of delirium in the intensive care unit: a survey of 912 healthcare professionals. *Crit Care Med* 2004; 32: 106-12.
12. Praditsuwat R, Sirisuwat A, Assanasen J, Eiamjinnasuwat W, Pakdeewongse S, Limmathuroskul D, et al. Short-term clinical outcomes in delirious older patients: A study at general medical wards in a university hospital in Thailand. *Geriatr Gerontol Int* 2013; 13:972-7.
13. Luetz A, Heymann A, Radtke FM, Chenitir C, Neuhaus U, Nachtigall I, et al. Different assessment tools for intensive care unit delirium: which score to use? *Crit Care Med* 2010; 38: 409-18.
14. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med* 2001;29:1370-9. See comment in PubMed Commons below
15. Girard TD, Pandharipande PP, Ely EW. Delirium in the intensive care unit. *Crit Care* 2008;12 Suppl 3:S3.
16. Pipanmekaporn T, Wongpakaran N, Mueankwan S, Dendumrongkul P, Chittawatanarat K, Khongpheng N, et al. Validity and reliability of the Thai version of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Clin Interv Aging* 2014;9: 879-85.
17. Siri S, Okanurak K, Chansirikanjana S, Kitayaporn D, Jorm AF. Modified Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) as a screening test for dementia for Thai elderly. *Southeast Asian J Trop Med Public Health* 2006;37:587-94.
18. Salluh JJ, Soares M, Teles JM, Ceraso D, Raimondi N, Nava VS, et al. Delirium epidemiology in critical care (DECCA): an international study. *Crit Care* 2010;14:R210.
19. Ely EW, Gautam S, Margolin R, Francis J, May L, Speroff T, et al. The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med* 2001;27:1892-900.
20. Cavallazzi R, Saad M, Marik P. Delirium in the ICU: an overview. *Ann Intensive Care* 2012;2:49.
21. Ouimet S, Kavanagh BP, Gottfried SB, Skrobik Y. Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med* 2007;33:66-73.
22. Chaiwat O, Chanidnuan M, Pancharoen W, Vijitmal K, Danpornprasert P, Toaditthep P, et al. Postoperative delirium in critically ill surgical patients: incidence, risk factors, and predictive scores. *BMC Anesthesiol*. 2019;19:39.
23. Rivers EP, Kruse JA, Jacobsen F, Shah K, Loomba M, Otero R, et al. The influence of early hemodynamic optimization on biomarker patterns of severe sepsis and septic shock. *Crit Care Med* 2007;35:2016-24.
24. Nguyen BH, Loomba M, Yang JJ. Early lactate clearance is associated with biomarkers of inflammation, coagulation, apoptosis, organ dysfunction and mortality in severe sepsis and septic shock. *J Inflamm (Lond)* 2010;7:6.
25. Permpikul C, Sringam P, Tongyoo S. Therapeutic goal achievements during severe sepsis and septic shock resuscitation and their association with patients' outcomes. *J Med Assoc Thai* 2014;97 Suppl 3:S176-S183.
26. Inouye SK, Rushing JT, Foreman MD, Palmer RM, Pompei P. Does delirium contribute to poor hospital outcomes? A three-site epidemiologic study. *J Gen Intern Med* 1998;13:234-42.
27. Girard TD, Jackson JC, Pandharipande P, Pun BT, Thompson JL, Shintani AK, et al. Delirium as a predictor of long term cognitive impairment in survivors of critical illness. *Crit Care Med* 2010;38:1513-20.