ORIGINAL ARTICLE

Assessment of Delirium as an Independent Predictor of Outcome among Critically Ill Patients in Intensive Care Unit: A Prospective Study

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Abstract

Background: Delirium is frequently observed among critically ill patients in the intensive care unit. Although a preventable and reversible process, it is associated with greater morbidity and mortality. Early recognition and interpreting the predisposing and precipitating risk factors for delirium can improve outcomes among these patients.

Objective: A prospective observational study was conducted with the primary objective to evaluate the incidence of delirium in a mixed adult intensive care unit. The secondary objectives were the evaluation of risk factors and outcomes of delirium.

Methods: All patients who were more than 18 years of age and with an ICU stay of more than 24 hours were included in the study. Patients with prior history of neurological disorders, psychosis, and who were deaf were excluded. Eligible patients were evaluated by the residents to detect delirium using confusion assessment method for the intensive care unit as a tool.

Results: A total of 110 patients were included, and delirium was detected in 41 patients (37.3%). Among the predisposing risk factors, only hypertension was significantly associated with delirium. Among precipitating factors, mechanical ventilation, use of physical restraints and presence of window/natural light exposure, high Acute Physiology and Chronic Health Evaluation II scores, use of opioids, and benzodiazepines were associated with delirium. In multivariate risk regression analysis, presence of window/natural light exposure {odds ratio (OR), 55.52; 95% CI (8.887–346.904)}; (p <0.001) and duration of stay in ICU OR (1.145); 95% CI (1.058–1.238) (p = 0.001) were independent risk factors of delirium. Also, high mortality (53.7%) was observed among the delirious group of patients.

Conclusion: Delirium is a common problem in the ICU and is associated with poor outcomes. Various risk factors are linked to ICU environment.

Keywords: Confusion assessment method for the intensive care unit, Delirium, Incidence, Intensive care unit, Risk factors.

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Introduction

Delirium is an acute impairment of consciousness producing a generalized cognitive impairment. Its course is fluctuating developing over a short period of time in the day. Delirium is reported to occur in 16 to 89% of critically ill patients in the ICU.[1]

It may be caused by a disease process that did not originate in the brain, such as infection (urinary tract infection or pneumonia) or drug effects, particularly anticholinergic or CNS depressants (benzodiazepines and opioids). Despite high prevalence rates in the ICU, delirium often remains unnoticed by the clinician. Most of the critically ill patients with delirium may either have hypoactive form or mixed form where they fluctuate between hyperactive and hypoactive forms.[2,3] Patients on mechanical ventilation in the ICU are at higher risk of developing delirium, pathogenesis of this is multifactorial and accounts for a longer stay in ICU and higher mortality.[4]

The primary objective was to evaluate the incidence of delirium among adult ICU patients using the confusion assessment method for the intensive care unit (CAM-ICU) and Richmond Agitation–Sedation Scale (RASS). The secondary objective was to evaluate the risk factors accounting to mortality and morbidity among delirious patients.

Methods

After Institutional Ethical Committee approval, this prospective and observational study was conducted on all patients aged above 18 years admitted to ICU of a tertiary care hospital for 9 months from May 2019 to February 2020. Written informed consent from the guardian of all patients was obtained. Family refusal, patients with prior history of psychosis, neurological disorder, unconscious, and deaf patients were excluded from the study.

All patients' information, comorbidities, medical history, drug history, and cause for ICU admission, was recorded at the time of admission in ICU. All patients were assessed twice daily in the morning (9 a.m.) and evening (5 p.m.). The endpoint was positive detection of delirium, discharge from ICU, or death in ICU. The patients were assessed on Acute Physiology and Chronic Health

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Evaluation II (APACHE II) scores, and the worst score within the first 24 hours was noted.

Richmond Agitation–Sedation Scale (RAAS) is a 10 point scale with scores from +1 to +4 assigned for levels of agitation through combativeness, 0—assigned for alert and calm state, −1 to −5 for depressed arousal or coma (Table 1).

CAM-ICU: It is a highly validated screening tool for delirium specifically in patients who cannot communicate verbally (mechanically ventilated)[5] (Figs 1 and 2).

Risk factors were assessed and classified into predisposing and precipitating factors. The predisposing factors, like comorbidities, e.g., hypertension, COPD, alcoholism, smoking, various medications, and diseases, may be present before the ICU admission. Precipitating factors are iatrogenic (mechanical ventilation, sedatives, presence near window, physical restraints, dyselectrolytemia) and related to the severity of illness.

Quantitative variables were compared using unpaired *t*-test/Mann–Whitney test, and qualitative variables were compared using chi-square test/Fisher's exact test. Univariate and multivariate logistic regression was done to find out significant risk factors of delirium. A $p < 0.05$ was considered statistically significant. The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0.

Results

During the study period, a total of 110 adult patients who fulfilled inclusion and exclusion criteria were assessed. Forty-one (37.3%) patients developed delirium during their stay in ICU.

Demographic profile was comparable in both groups (Table 2). Patients with admissions from the medical ward (63.4%) were found to be significant ($p = 0.015$) in delirious group with higher comorbidities (Table 3).

Among the predisposing factors, only history of hypertension (31.7 vs 14.5%; $p = 0.035$) was significant in the development of delirium, while others were not.

With regard to precipitating risk factors, high APACHE II scores (15.07 ± 5.99 vs 9.16 ± 7.18; $p < 0.001$), use of benzodiazepine i.v midazolam 1 mg more than once in their stay (29.3 vs 13.3%; $p = 0.040$), opioids i.v morphine 100 μg/kg/fentanyl 1 to 2 μg/kg (80.5 vs 27.5%; $p < 0.001$), sepsis (39 vs 14.5%; $p = 0.004$), presence of window/natural light exposure (12.2 vs 91.3%; $p < 0.001$), need/

Table 1: The Richmond Agitation–Sedation Scale (RASS)

Score	*Term*	*Description*
+4	Combative	Overly combative or violent: immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient-ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
−1	Drowsy	Not fully alert but has sustained (more than 10 seconds) awakening, with eye contact, to voice
−2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
−3	Moderate sedation	Any movement (but no eye contact) to voice
−4	Deep sedation	No response to voice, but any movement to physical stimulation
−5	Unarousable	No response to voice or physical stimulation

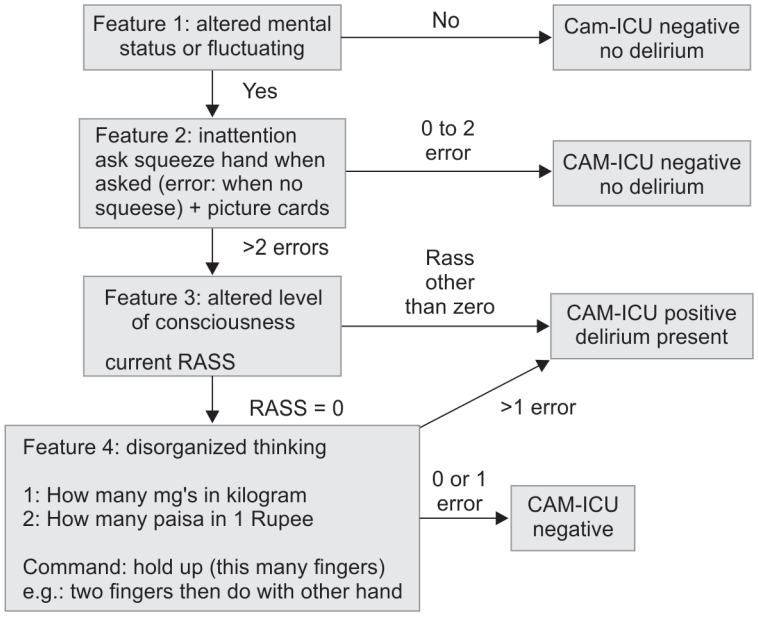

Fig. 1: Flow diagram to assess CAM-ICU

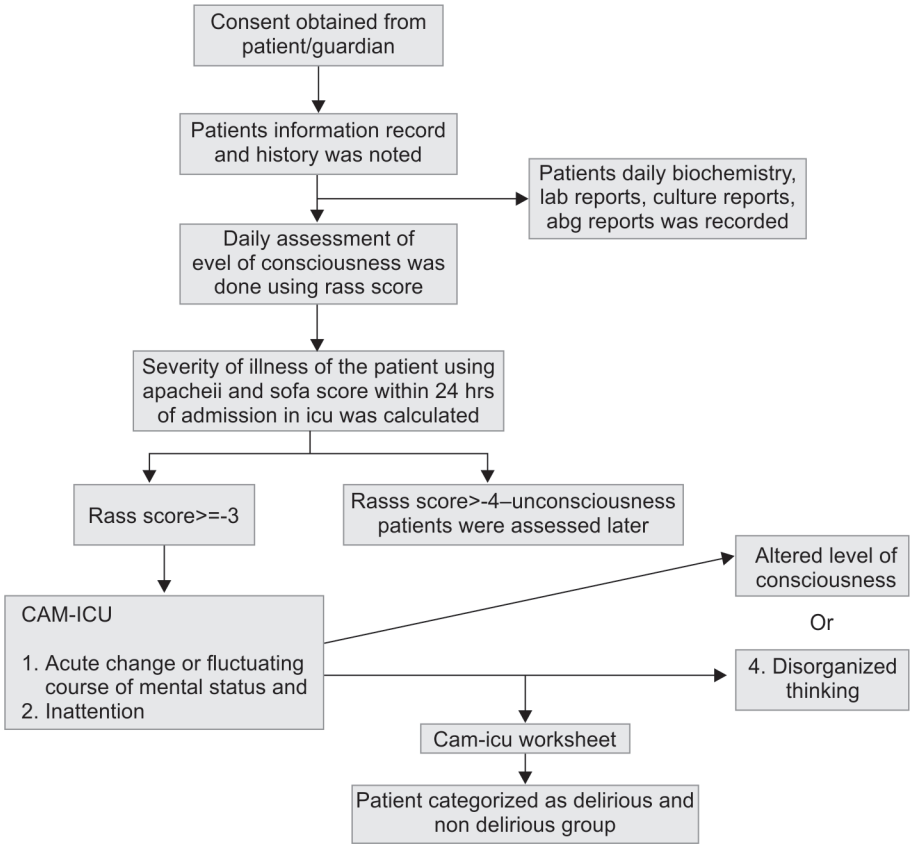

Fig. 2: Flowchart depicting the steps of data collection

use for physical restraints (78 vs 4.3%; p <0.001), mechanical ventilation (97.6 vs 55.1%; p <0.001) with duration of mechanical ventilation [20.3 ± 11.6; median, 16 days; interquartile range (IQR), 11 vs 6.5 ± 9.4; median, 4 days; IQR, 5], duration of ICU stay (median of 18 days; IQR, 15–24 days vs median of 4 days; IQR, 3–6 days; p <0.001) were found significant in the development of delirium. Higher mortality was noted among the delirious group of patients (53.7%) (Table 2).

Logistic regression (Table 4) was performed to determine the independent predictors of delirium. Exposure to window/natural light odds ratio (OR) (55.526); 95% CI (8.887–346.904); (p <0.001) and duration of stay in ICU OR (1.145); 95% CI (1.058–1.238); (p = 0.001) were the significant independent factor.

Discussion

ICU is a distinctive ward as patients herein are more moribund, experience many physical and psychological stress besides their physical environment which may contribute to delirium. The reported incidence of delirium in ICU varies from 16 to 60%.[1,6-11] Using RASS and CAM-ICU tools for evaluation in our study, the incidence of delirium was 37.3%. This wide range of variations in the incidence could be due to the type of ICU settings (cardiac, surgical, and respiratory), and various tools used to assess delirium interpretation, local sedation practices, and confounding factors.

Though the etiology of delirium is complex, various precipitating and predisposing factors can influence to cause delirium. Predisposing factors, like comorbidities, alcoholism, smoking, various medications, may be present before the ICU admission and can rarely be modifiable, whereas precipitating factors like mechanical ventilation, sedatives, presence near the window, physical restraints, dyselectrolytemia and related to the severity of illness which are modifiable.

Of the predisposing risk factors, hypertension (p = 0.035) was significantly associated with the development of delirium in our study. Similarly, Ouimet et al. (OR, 1.88; 95% CI, 1.3–2.6)[1] and Dubois et al.[12] too linked hypertension to the development of delirium.

In hypertensive patients, damage to vascular structures leading to hypoperfusion of cerebral structures and causing cerebral hypoxia makes them at high risk for delirium when admitted in the ICU.[13] Further, chronic hypertension has been associated with impairment in memory, attention and abstract reasoning may be the reason for increased occurrence of delirium in these patients.

While other predisposing factors, like fever, smoking, tobacco consumption, use of steroids, dyselectrolytemia, COPD or diabetes mellitus, did not account for delirium in our study. On the contrary Ouimet et al.[1] and Van Rompaey et al.[14] found that smoking the contrary was associated with delirium.

Delirium was observed to be higher among patients (80%) who were transferred from the medical ward. More comorbidities, higher APACHE scores, and complex courses may have contributed to the development of delirium among patients with a medical cause. Van Rompaey et al.[14] also found a similar association that patients with chronic diseases developed delirium more than surgical patients.

Among the precipitating factors, patients with higher APACHE II scores (15.07 + 5.99 vs 9.16 + 7.8; p <0.001) manifested delirium significantly. Romapaey et al. too found that higher

Table 2: General characteristics and risk factors for development of delirium

Variables	*Delirium group (N = 41) N (%)*	*Nondelirium group (N = 69) N (%)*	*p value*
Age (mean ± SD (years))	38.1 ± 16.3	39.4 ± 14.7	0.67
Sex (male/female)	26/15 (63.4%/36.6%)	46/23 (66.7%/33.3%)	0.65
Mode of admission	26 (63.4%)	24 (34.8%)	0.015
Medical ward	8 (19.5%)	27 (39.1%)	
Surgical ward	7 (17.1%)	18 (26.1%)	
Trauma			
Predisposing factors			
Smoking history			0.58
Alcohol history	16 (39%)	23 (33.3%)	0.60
Tobacco history	22 (53.7%)	33 (47.8%)	0.56
Hypertension	4 (9.8%)	10 (14.5%)	0.03
COPD	13 (31.7%)	10 (14.5%)	1.00
Diabetes	4 (9.8%)	6 (8.7%)	0.33
Tuberculosis	9 (22%)	10 (14.5%)	0.08
Epilepsy	Nil	6 (8.7%)	0.70
Thyroid dysfunction	2 (4.9%)	5 (7.2%)	1.00
Coronary artery disease	3 (7.3%)	4 (5.8%)	0.52
Precipitating factors	Nil	2 (2.9%)	
APACHE II score			<0.001
SOFA score	15 ± 5.9	9.2 ± 7.2	<0.001
Hypotension	8.2 ± 6.0	4.3 ± 3.2	0.54
Benzodiazepine (i.v midazolam)	8 (19.5%)	13 (18.8%)	0.04
Steroids	12 (29.3%)	9 (13%)	0.17
Opioids (i.v morphine/fentanyl)	25 (61%)	29 (42%)	<0.001
Sepsis	33 (80.5%)	19 (27.5%)	0.004
Nasogastric feeds	16 (39%)	10 (14.5%)	0.07
Foleys catheterization	30 (73.2%)	38 (55.1%)	0.45
Window/natural light exposure	37 (90.2%)	59 (85.5%)	<0.001
Physical restraints	5 (12.2%)	63 (91.3%)	<0.001
Mechanical ventilation	32 (78%)	3 (4.3%)	<0.001
No. of days on mechanical ventilation (IQR)	40 (97.6%)	38 (55.1)	
Duration of stay (IQR)	20.3 ± 11.6 (11)	3.95 ± 7.92 (4.5)	<0.001
Mortality in ICU	25.00 ± 17.80 (3–6)	6.03 ± 7.76 (15–24)	
	22(53.6%)	20(29%)	

SD, standard deviation; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; i.v, intravenous; IQR, interquartile range

Table 3: Association of comorbidity with delirium among patients admitted from ward

Ward	*Delirium with comorbidity (N) (%)*	*Delirium without comorbidity (N) (%)*	*Nondelirium with comorbidity (N) (%)*	*Nondelirium without comorbidity (N) (%)*	*p value*
Medical	21 (80%)	5 (20%)	9 (37.5%)	15 (62.5%)	**0.001**
Surgical	5	3	17	10	0.98
Trauma	5	2	17	1	0.111
Total	31	10	43	26	

APACHE II scores (≥24 scores) were associated with delirium.[14] Ouimet et al. (17.9 ± 8.2 vs 14.0 ± 8.0; p <0.0001),[1] Ely et al.,[4] and Thomason et al.[9] too reported delirium to be associated with high APACHE II scores but not with increased age, sex, and race. On the contrary, Thomason et al.[9] and Sharma et al.[15] have linked higher APACHE II scores with increased age in the development of delirium.

Among medications, benzodiazepines (midazolam) and opioids (morphine/fentanyl) usages were significantly associated with the development of delirium. Studies from Sharma et al.[14] and Lahariaya et al.[16] too concur with our findings.

Benzodiazepines increase the level of GABA, which results in an increase in sedation and it is a common practice in ICU to manage behavioral problems with benzodiazepines and opioids, so the use of medications was an important predictor of delirium. Hence, sedation should be used judiciously in ICU.

In the literature, sepsis-associated delirium is often observed in the early stages of sepsis. Its prevalence varies from 9 to 71% of patients with severe sepsis.[17] The potential mechanisms for sepsis-associated delirium include vascular damage, endothelial activation, breakdown of the blood-brain barrier, metabolic disorders, brain inflammation, and apoptosis. We too found a strong association of sepsis with delirium. Sixteen out of 41 (39%) patients who had sepsis exhibited delirium (p = 0.004) in our study.

Unfamiliar environment, sleep deprivation, loss of day and night awareness, and noncommunication with their caregivers

Table 4: Logistic regression to determine the independent predictors of delirium using the enter method

				95.0% C.I.	
	B	*p value*	*OR*	*Lower*	*Upper*
APACHE II	0.034	0.59	1.034	0.91	1.17
Benzodiazepine	1.514	0.13	4.54	0.61	33.75
Sepsis	0.376	0.69	1.45	0.21	9.78
Opioids	−1.39	0.19	0.24	0.03	2.03
Window/natural light	4.017	**<0.001**	55.52	8.88	**34.69**
Duration of stay	0.135	**0.001**	1.145	1.058	1.23
Constant	−5.772	0.003	0.003		

OR, odds ratio

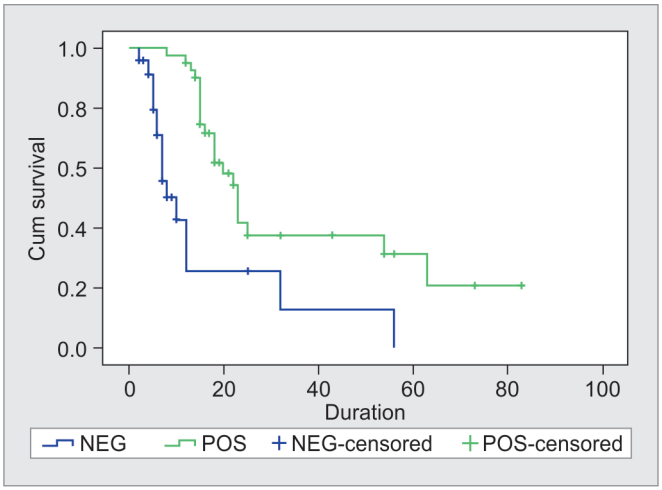

Fig. 3: Kaplan–Meier analysis depicting the impact of delirium on mortality among two groups in the intensive care unit. *X* axis represents the duration of stay (days) in ICU

may result in anxiety among critically ill patients in ICU. Majority of the time, clinician either fails to detect or ignores it or when detected may label it as ICU psychosis. Hence it should be a part of the regular armamentarium of ICU rounds to recognize any anxiety among patients.

In our study, the patients who were not exposed to natural light via windows developed delirium more as compared to those in nondelirious group. Absence of light or windowless room in ICU has been reported as risk factor for manifestation of delirium.[8,12] A study by Smonig et al.[18] showed that admitting patients to a room with windows or daylight exposure seemed to have a protective effect on episodes of agitation.

Around 78% of patients, who had physical restraints, developed delirium in our study. This also resulted in critical events like self-removal of endotracheal tubes and various invasive catheters. Our results were higher than Pan et al. (39.8%)[19] but similar to Rompaey et al. OR (33.84).[8]

Mechanical ventilation has been shown to have a strong evidence as an important precipitating factor for delirium.[20]

Almost, 97% of patients on mechanical ventilation were associated with delirium. The duration of mechanical ventilation among them was (20.3 ± 11.6; median, 16 days; IQR, 11 vs 6.5 ± 9.4; median, 4 days; IQR, 5 days), which was higher in our study when compared to study by Lat et al.[20] Ely et al.[2] have reported delirium in 32.4% of patients on mechanical ventilation, which was lower than our study. Higher comorbidities, sepsis with higher APACHE II, and overzealous use of narcotics and benzodiazepines may be the reason for the longer duration of mechanical ventilation. Also, complication such as pulling out of endotracheal tube due to agitation in delirious patients further increased the duration of mechanical ventilation and longer ICU stay. However, we did not record the complications as a consequence of delirium among these patients in this study.

The mean duration of stay among delirious patients in the ICU was {25.00 ± 17.80 (IQR, 2–6) vs 6.03 ± 7.76 (IQR, 15–24) days}. This is supported by the findings from other studies that delirium was associated with prolonged ICU stay and high mortality 53.7%.[9,14,15, 21,22] However, it remains unclear whether delirium directly causes death or reflects severity of illness as there were many confounding factors that can precipitate delirium as well as are responsible for death. In fact, there has been no in-depth analysis focusing on the direct contribution of delirium to clinical outcomes in critically ill ICU patients.[2]

Using logistic regression, exposure to window/natural light OR (55.526); 95% CI (8.887–346.904); (p <0.001) and duration of stay in ICU OR (1.145); 95% CI (1.058–1.238); (p = 0.001) were significantly the independent predictors of delirium. The fact that delirium was an independent determinant of length of stay in ICU reflects that it is poorly monitored and not uncommon complication in the ICU and thus must be given a high priority.[23]

The strength of our study was a twice daily assessment of delirium using CAM-ICU and RASS. Further, patients, who were diagnosed, were treated early like reorientation and behavioral intervention of patients by the caregivers by frequent visiting and judicious use or even policy of no sedative and antipsychotics (haloperidol/risperidone).

This study has limitations such as small size, assessment of delirium was not done at fixed time and, we might have missed as it has a fluctuating course. The present study excluded the patients who had visual and auditory impairments who are also at high risk for exhibiting delirium. Factors like doses of sedatives were not evaluated to dose risk relationship. The side effects of antipsychotics were not recorded which was the drawback in our study. Also, further studies should be done to focus on the prevention and treatment of delirium that would modify the clinical outcome including mortality, length of stay, and long-term neuropsychological outcomes.

Conclusion

The incidence of delirium was 37.3% among adult patients in the ICU with higher morbidity and mortality as high as 53.7% in our study. Good monitoring, early recognition of delirium, and subsequent early intervention can improve the outcome of patients in ICU.

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References

1. Ouimet S, Kavanagh BP, Gottfried SB, Skobik Y. Incidence, risk factors and consequences of ICU delirium. Intensive Care Med 2007;33(1):66–73. DOI: 10.1007/s00134-006-0399-8.
2. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harell FE, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. J Am Med Assoc 2004;291(14):1753–1762. DOI: 10.1001/jama.291.14.1753.
3. Devlin JW, Fong JJ, Fraser GL, Riker RR. Delirium assessment in the critically ill. Intensive Care Med 2007;33(6):929–940. DOI: 10.1007/s00134-007-0603-5.
4. 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(1):106–112. DOI: 10.1097/01.CCM.0000098033.94737.84.
5. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). J Am Med Assoc 2001;286(21):2703–2710. DOI: 10.1001/jama.286.21.2703.
6. Grover S, Subodh BN, Avasthi A, Chakrabarti S, Kumar S, Sharan P, et al. Prevalence and clinical profile of delirium: a study from a tertiary-care hospital in north India. Gen Hosp Psychiatry 2009;31(1):25–29. DOI: 10.1016/j.genhosppsych.2008.06.001.
7. Krewulak KD, Stelfox HT, Leigh JP, Ely EW, Fiest KM. Incidence and prevalence of delirium subtypes in an adult ICU: a systematic review and meta-analysis. Crit Care Med 2018;46(12):2029–2035. DOI: 10.1097/CCM.0000000000003402.
8. Rompaey BV, Schuurmans MJ, Shortridge-Baggett LM, Truijen S, Elseviers M, Bossaert L. A comparison of the CAM-ICU and the NEECHAM Confusion Scale in intensive care delirium assessment: an observational study in non-intubated patients. Crit Care 2008;12(1):R16. DOI: 10.1186/cc6790.
9. Thomason JW, Shintani A, Peterson JF, Pun BT, Jackson JC, Ely EW. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. Crit Care 2005;9(4):R375–R381. DOI: 10.1186/cc3729.
10. George C, Nair JS, Ebenezer JA, Gangadharan A, Christudas A, Gnanaseelan LK, et al. Validation of the intensive care delirium screening checklist in nonintubated intensive care unit patients in a resource-poor medical intensive care setting in South India. J Crit Care 2011;26(2):138–143. DOI: 10.1016/j.jcrc.2010.11.002.
11. Bamalwa M, Mahmood SN, Praharaj SK. Delirium in cardiac ICU patients. Ann Clin Psychiatry 2016;28(1):51–55 PMID is 26855986.
12. 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(8):1297–1304. DOI: 10.1007/s001340101017.
13. Waldstein SR, Manuck SB, Ryan CM, Muldoon MF. Neuropsychological correlates of hypertension: Review and methodologic considerations. Psychol Bull 1991;110(3):451–468. DOI: 10.1037/0033-2909.110.3.451.
14. Van Rompaey B, Elseviers MM, Schuurmans MJ, Shortridge-Baggett LM, Truijen S, Bossaert L. Risk factors for delirium in intensive care patients: a prospective cohort study. Crit Care 2009;13(3):R77. DOI: 10.1186/cc7892.
15. Sharma A, Malhotra S, Grover S, Jindal SK. Incidence, prevalence, Risk factor and outcome of delirium in intensive care unit: a study from India. Gen Hosp Psych 2012;34(6):639–646. DOI: 10.1016/j.genhosppsych.2012.06.009.
16. Lahariaya S, Grover S, Bagga S, Sharma A. Delirium in patients admitted to a cardiac Intensive care unit with cardiac emergencies in a developing country: incidence, prevalence, risk factor and outcome. Gen Hosp Psych 2014;36(2):156–164. DOI: 10.1016/j.genhosppsych.2013.10.010.
17. Ebersoldt M, Sharshar T, Annane D. Sepsis-associated delirium. Intensive Care Med 2007;33(6):941–950. DOI: 10.1007/s00134-007-0622-2.
18. Smonig R, Magalhaes E, Bouadma L, Andremont O, Montmollin E, Essardy F, et al. Impact of natural light exposure on delirium burden in adult patients receiving invasive mechanical ventilation in the ICU: a prospective study. Ann Intensive Care 2019;9(1):120. DOI: 10.1186/s13613-019-0592-x.
19. Pan Y, Jiang Z, Yuan C, Wang L, Zhou J, Tao M, et al. Influence of physical restraints on delirium of adult patients in ICU. A nested case-control study. J Clin Nurs 2018;27(9–10):1950–1957. DOI: 10.1111/jocn.14334.
20. Lat I, McMillian W, Taylor S, Janzen JM, Papadopoulos S, Korth L, et al. The impact of delirium on clinical outcomes in mechanically ventilated surgical and trauma patients. Crit Care Med 2009;37(6):1898–1905. DOI: 10.1097/CCM.0b013e31819ffe38.
21. Aldemir M, Ozen S, Kara IH, Sir A, Bac B. Predisposing factors for delirium in the surgical intensive care unit. Crit Care 2001;5(5):265–270. DOI: 10.1186/cc1044.
22. Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomised controlled trial. Lancet 2008;371(9607):126–134. DOI: 10.1016/S0140-6736(08)60105-1.
23. 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(12):1892–1900. DOI: 10.1007/s00134-001-1132-2.