Research Article

Delirium as a predictor of longer hospital stays in mechanically ventilated patients

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Abstract

Background: Respiratory failure is one condition that needs mechanical ventilation in the intensive care unit (ICU). Patients in the ICU are highly vulnerable to the development of delirium due to various reasons. Delirium is associated with more deaths, longer ICU stay, and higher cost.

Objective: This study was carried out to determine the relationship between delirium and length of stay in ICU and hospital among mechanically ventilated ICU patients.

Materials and Methods: This was a prospective study, conducted on 105 consecutively admitted medical ICU patients requiring mechanical ventilation during hospitalization from 1 June 2013 to 1 may 2014. We assessed delirium using the Confusion Assessment Method for the ICU and Richmond Agitation–Sedation Scale. Cox proportional hazards regression analysis was used to assess the effects of delirium and to determine the relationship between delirium and its variables.

Results: Of 105 patients, 48 (45%) patients experienced delirium. Patients who experienced delirium were older in age (mean ± SD: 54 ± 16 versus 47 ± 15 years) compared to their counterparts who did not experience delirium. They had a 39% greater risk of remaining in the ICU on any given day even after adjusting for age, gender, race, Charlson comorbidity score, APACHE II score, and coma (HR: 1.12; 95% CI: 0.83–1.52, $p = 0.06$). Similarly, patients who experienced delirium had a 45% greater risk of remaining in the hospital after adjusting for the same covariates (HR: 1.9; 95% CI 1.3–2.9; $p < 0.01$).

Conclusion: In this study, delirium occurred in nearly half of the mechanically ventilated ICU patients. Even after adjustment for relevant covariates, delirium patients had longer ICU and hospital stay. So delirium is found to be a predictor of longer hospital stays in mechanically ventilated patients.

KEY WORDS: Delirium, mechanical ventilation, intensive care unit (ICU)

Introduction

Respiratory failure is one of the conditions that need mechanical ventilation in patients admitted in ICU. Though advances in critical care medicine have decreased the morbidity and mortality of the patients in intensive care units (ICUs) worldwide, delirium has received little attention in ICU settings. Patients in the ICU are highly vulnerable to the development of delirium because of long-term illness, multiorgan failure, use of medications, and other environmental factors.[1]

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Delirium is defined as disturbance of consciousness and cognition that develops over a short period of time (hours to days) and fluctuates over time. This is a common manifestation of acute brain dysfunction in critically ill patients, occurring in most of patients admitted to the ICU. Delirium is an organic dysfunction having multifactorial origin[2,3] with complex pathophysiology, including inflammatory response of the brain to injury, hormonal influences and changes in neurotransmission, and neural network connectivity.[1,4] It is more common in the elderly patients due to aging of the brain and can be classified easily using *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, of the American Psychiatric

Association (APA).[5,6] Different terms were used to describe delirium as cognitive impairment in critically ill patients, including ICU psychosis, ICU syndrome, acute confusional state, encephalopathy, and acute brain failure.[1,7] However, the critical care literature has recently confirmed the recommendations of the APA and other experts that the term *delirium* be used uniformly to describe this syndrome of brain dysfunction. As dysfunction of the other organ systems is receiving more attention in the present scenario, delirium should also be recognized as a principal contributor to morbidity and mortality in the ICU. It is recommended to monitor all ICU patients for this complication, as in some of the tertiary care centers. Patients with delirium have longer hospital stays than those without delirium, and preliminary research suggests that delirium may be associated with cognitive impairment that persists months to years, even after discharge.

The impact of delirium on critically ill patients has been greatly studied, as its occurrence is an independent predictor of assessing mortality, duration of mechanical ventilation, long-term complications in the ICU, and length of stay in the hospital for patients with posttraumatic stress disorder.[8–10] The incidence of delirium in ICU patients ranges from 45% to 87%. The original Confusion Assessment Method of Inouye et al.[11] has popularized the monitoring of delirium by non-psychiatrists. Recently, this method has become the most valid and reliable tool to measure delirium[2,12–14] in the ICU patients.

In intensive care unit, delirium is a common condition yet underdiagnosed form of organ dysfunction, and its contribution to patient outcomes is unclear. Therefore, we undertook this study to test the hypothesis that delirium in the ICU is a predictor of length of stay among patients with respiratory failure requiring mechanical ventilator support and to determine the impact of delirium on the length of stay in ICU and hospital even after adjusting for other covariates.

Materials and Methods

This prospective study was conducted in Siddhartha Medical College and Government General Hospital, Vijayawada, Andhra Pradesh, India. It is an observational cohort study[15] approved by the Departmental Research Committee. Informed consent was obtained from the patients or their relatives. Study was carried out during a period of 11-month interval from 1 June 2013 to 1 May 2014, on 105 patients admitted to the ICU and met the inclusion criteria. The inclusion criteria included patients aged 18–80 years who were admitted in the medical ICU for more than 24 h and required mechanical ventilation. They were followed up until hospital discharge. The exclusion criteria included patients with known history of psychosis or neurological diseases that could confound to delirium and comatose patients.

We assessed the sedation level using Richmond Agitation–Sedation Scale[16,17] and delirium status using Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).[13,14] These data were recorded prospectively at least once per 12-h shift as part of routine rounds. Information collected prospectively at the time of enrollment included patient demographics, severity of illness assessed using the Acute Physiology and Chronic Health Evaluation II (APACHE II)[18] score, and admission diagnoses. The Charlson Comorbidity Index, which takes into account the number and seriousness of preexisting comorbid conditions, was calculated using ICD-9 codes as per Deyo et al.[19] The diagnostic categories for ICU admission were recorded by medical teams and decided for ICU admission.

Delirium in the ICU is an independent variable in this study.[13,14] Patients who scored positive for delirium by the CAM-ICU at any time while in the ICU were categorized as “with Delirium.” All others were categorized as “without Delirium.” The two variables included length of stay in the ICU and in the hospital.

Statistical analyses were carried out using Fisher’s test and $\chi 2$-test to determine the differences in baseline features between those with and without delirium. Cox proportional hazards regression analysis[20] was used to assess the effects of delirium on ICU length of stay and hospital length of the stay. To analyze the relationship between delirium and its variables, delirium was considered as a time-dependent variable in days. ”Day 0” is considered as the day on which first delirious event occurred and the days were counted from then onwards. Other baseline covariates included in each model were age, gender, APACHE II score, and Charlson Comorbidity Index. Time-to-event curves were created by Kaplan–Meier plots.[21] All statistical analyses were conducted using GraphPad Prism for Windows, version 5.04.

Results

This study included 105 patients, in which 48 (45%) patients experienced delirium. Baseline characteristics of the patients are presented, with the cohort divided into two groups: with delirium (n = 48) and without delirium (n = 57). There were no significant differences between the with-delirium and without-delirium groups for age and gender. Primary medical diagnoses were similar between the groups, respiratory (e.g., chronic obstructive pulmonary disease exacerbation) and metabolic (e.g., drug overdose, diabetic ketoacidosis) syndromes being the most common reasons for admission to the ICU.

Results indicate that with-delirium group stayed in the ICU 2 days longer (median days 5; interquartile range (IQR) 4–6 versus median days 3; IQR 2–4) and had 39% greater risk of remaining in the ICU than without-delirium group. The hospital stay of the with-delirium group was 8 days longer and had a 45% greater risk of remaining in the hospital (median days 18; IQR 16–22 versus median days 10; IQR 6–13) than that of without-delirium group.

Discussion

In the 11-month study period, 300 mechanically ventilated ICU patients were admitted, of which only 105 (35%) patients

Table 1: Patient demographics

Characteristic	With delirium (*n* = 48)	Without delirium (*n* = 57)
Mean age (±SD) (years)	54 (±16)	47 (±15)
Males (%)	22 (50)	27 (50)
Charlson Comorbidity Index, mean (± SD)	3.1 (± 2.8)	3.1 (± 2.8)
APACHE II score, mean (± SD)	22.2 (±9.4)	24.5 (±7.9)

Table 2: Diagnostic category for ICU admission

Diagnosis	With delirium (*n* = 48)	Without delirium (*n* = 57)
Respiratory	13	25
Metabolic syndrome	15	90
Gastrointestinal	8	13
Cardiac	4	6
Cancers	2	2
Renal	5	1
Other	1	1
Total	48	57

who met the inclusion criteria were considered for the study and the remaining 195 (65%) patients were excluded (Table 1). On enrollment, 57 (55%) patients were defined as normal and 48 (45%) were defined as delirious. Table 2 shows the proportion of patients in each diagnosed category. Enrolled patients had a mean age of 54 ± 16 years in with-delirium and 47 ± 15 years in the without-delirium groups. The mean values of the patients with similar baseline characteristics of greater severity of illness at the enrollment as measured by APACHE II scores were 22.2 ± 9.4 in with-delirium and 24.5 ± 7.9 in without-delirium groups. The Charlson Comorbidity Index was 3.1 ± 2.8 in both with-delirium and without-delirium patients. There were no significant differences between the with-delirium and without-delirium groups for baseline comorbidities, severity of illness scores, or admission diagnoses.

In this study, nearly half (48%) of the patients developed delirium, which was associated with 2-day longer ICU stay and 8-day longer in-hospital stay. Patients who experienced delirium had a 39% greater risk of remaining in the ICU on any given day, even after adjusting for age, gender, race, Charlson comorbidity score, APACHE II score (Table 3; HR: 1.12; 95% CI: 0.83–1.52, $p = 0.06$). Similarly, patients who experienced delirium had a 45% greater risk of remaining

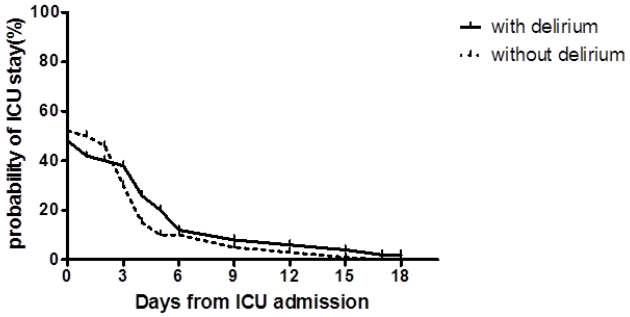

Figure 1: Kaplan–Meier plot showing relation between delirium and length of stay in ICU with delirium versus without delirium

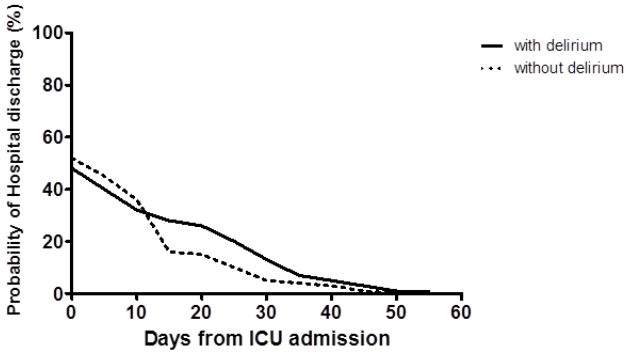

Figure 2: Kaplan–Meier plot showing the relationship between delirium and length of stay in hospital with delirium versus without delirium

in the hospital after adjusting for the same covariates (Table 3; HR: 1.9; 95% CI: 1.3–2.9; $p < 0.01$). There was high prevalence of delirium among the mechanically ventilated adults admitted in both ICU and hospital. This study supports the Society of Critical Care Medicine clinical practice guidelines recommendation[22] for routine monitoring of delirium for all adult ICU patients, using validated tools such as the CAM-ICU in critically ill patients.[13,14] Monitoring delirium with the CAM-ICU is easy on daily basis and takes only 1–2 min. It allows the medical professionals to consider the causes and modify treatment accordingly in those who experience delirium.[23,24] Kaplan–Meier plots (Figures 1 and 2),

Table 3: Clinical outcome and multivariable analysis

Length of stay	With delirium (*n* = 48)	Without delirium (*n* = 57)	Hazards ratio* (95% CI)	*p*-Value
ICU	5 (4,6)	3 (2,4)	1.12 (0.83–1.52)	0.06
In hospital	18 (16,22)	10 (6,13)	1.9 (1.3–2.9)	<0.01

*Hazard ratios and *p*-values taken from multivariable Cox proportional hazards regression models adjusting for age, gender, race, APACHE II score, and Charlson Comorbidity Index. ICU and hospital lengths of stay expressed as median days with interquartile ranges. ICU, intensive care unit; CI, confidence interval.

which show the relationship between delirium and length of stay, analyze that the duration of delirium found after adjusting for covariates with each additional day spent in delirium by an ICU patient is associated with increased risk of remaining in the hospital or in the wards. Patients with respiratory failure requiring mechanical ventilator support were at significantly higher risk, once they were delirious in their disease course. Compatible with previous reports, our results also indicated that APACHE III score,[18,25–27] the presence of shock[28] and development of delirium[6] were highly related to mortality in mechanically ventilated patients. Thus, similar to APACHE III score, delirium should be recognized as a marker for evaluating illness severity in patients with respiratory failure. Previous research has shown the importance of delirium as a prognostic predictor of both in-hospital[29,30] and 12-month mortality[31] among patients not admitted to the ICU.

This study used the CAM-ICU to nonverbally evaluate the presence of delirium in patients with mechanical ventilator support. The CAM-ICU has been reported as a tool with high reliability, showing excellent integrated agreement.[13,14] A recent article also showed that development of delirium in patients receiving mechanical ventilation at some point during the ICU stay is an independent predictor of higher 6-month mortality and longer hospital stay.[2] Similarly, the results of our study revealed that development of delirium in mechanically ventilated patients during their course of ICU stay increased the in-hospital stay. Therefore, detection of delirium in mechanically ventilated patients should prompt efforts to identify and treat the modifiable factors associated with mortality.[3]

Perhaps the greatest benefit of incorporating delirium monitoring would be the enhanced detection of the hypoactive delirium subtype, which is characterized by a flat affect or apathy and often present in otherwise calm and seemingly alert patients.[32] This is in contrast to the readily detected hyperactive delirium that is characterized by restlessness, attempting to remove catheters or tubes, beating, biting, and emotional upset.[32] In this study, hypoactive delirium was present in more than 60% patients with normal or near-normal arousal. Hypoactive delirium has bad prognosis than hyperactive delirium and is the most commonly missed subtype of delirium. Considering that symptoms of ICU delirium are largely hypoactive rather than hyperactive,[12,33] anything short of objective looking for delirium will result in undetected brain dysfunction.

The development of delirium in mechanically ventilated patients is associated with an increased length of ICU and hospital stay. Our study was not prospectively powered to determine a definitive relationship between delirium and mortality. Mortality analysis was not carried out because the ICU patients had a lower severity of illness than those in the prior ICU studies, isolated to ventilated patients. The myriad of data in other non-ICU population showed that delirium is associated with prolonged stay, greater dependency of care, and subsequent institutionalization.[30,31,33–37]

Every study has its own limitations, likewise in the present study, mortality was not noted and there was no tool to stratify the severity of delirium. Currently, there is no validated measure to stratify the severity of delirium even though the work in this area is ongoing. Third, a recurrent limitation in all cohort studies is that there may be unknown covariates that influence outcomes.

Ultimately, further research incorporating a randomized, prospective clinical trial focusing on the prevention and treatment of delirium will be necessary to confirm such a relationship. Data from other investigations, however, suggest that such a cause-and-effect relationship between delirium and negative clinical outcomes exists.

Conclusion

In this observational study we found that delirium among mechanically ventilated patients in the ICU is associated with longer lengths of stay, even after adjusting for covariates. It can be considered that validated instruments can be administered with a high degree of reproducibility and rates of compliance at the bedside by those routinely caring for patients in the ICU. Further studies are needed to determine whether prevention or treatment of delirium would change clinical outcomes including length of stay, cost of care, and long-term neuropsychological outcomes among survivors of critical illness.

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References

1. McGuire BE, Basten CJ, Ryan CJ, Gallagher J. Intensive care unit syndrome: a dangerous misnomer. Arch Intern Med 2000;160:906–09.
2. 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;27:1892–1900.
3. 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.
4. 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.
5. Rothschild JM, Leape LL. *The Nature and Extent of Medical Injury in Older Patients*. Washington, DC: The Public Policy Institute, 2000. Available at: http://assets. aarp.org/ rgcenter/ health/2000_17_injury.pdf
6. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition, text revision. Washington, DC: American Psychiatric Association, 2000.
7. Justic M. Does “ICU psychosis” really exist? Crit Care Nurse 2000;20:28–37.

8. Y. Shehabi, Riker RR, Bokesch PM, Wisemandle W, Shintani A, and Ely EW. Delirium duration and mortality in lightly sedated, mechanically ventilated intensive care patients. Crit Care Med 2010;38(12)2311–18.
9. Herrejón P. [Diagnosis of delirium in the critical ill]. Medicina Intensiva 2010;34(1):1–3.
10. Bäckman JC, Capuzzo M, Flaatten H, Rylander C, Griffiths RD. Precipitants of post-traumatic stress disorder following intensive care: a hypothesis generating study of diversity in care. Intensive Care Med 2007;33(6):978–85.
11. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horowitz RI. Clarifying confusion: the confusion assessment method. Ann Intern Med 1990;113:941–8.
12. 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.
13. 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). JAMA 2001;286:2703–10.
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.
15. Truman B, Shintani A, Jackson J, Peterson JF, Thomason J, Ely EW. Implementation of the SCCM guidelines for sedation and delirium monitoring in the ICU. Am J Respir Crit Care Med 2003;167:A969.
16. Sessler CN, Gosnell M, Grap MJ, Brophy GT, O'Neal PV, Keane KA et al. The Richmond Agitation–Sedation Scale: validity and reliability in adult intensive care patients. Am J Respir Crit Care Med 2002;166:1338–44.
17. Ely EW, Truman B, Shintani A, Thomason JWW, Wheeler AP, Gordon S et al. Monitoring sedation status over time in ICU patients: the reliability and validity of the Richmond Agitation Sedation Scale (RASS) J Am Med Assoc 2003;289:2983–91.
18. Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG et al. The APACHE III prognostic system: risk prediction of hospital mortality for critically ill hospitalized adults. Chest 1991;100:1619–36.
19. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613–19.
20. Altman DG, Andersen PK. Bootstrap investigation of the stability of a Cox regression model. Stat Med 2003;8:771–83.
21. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–81.
22. Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med 2002;30:119–41.
23. American Psychiatric Association. Practice guidelines for the treatment of patients with delirium. Am J Psychiatry 1999;156(Suppl):1–20.
24. American Psychiatric Association. What is Delirium? Available at: http://www.psych.org/psych_pract/treatg/patientfam_guide/Delirium.pdf (last accessed on March 9, 2004).
25. Wagner DP, Knaus WA, Harrell FE, Zimmerman JE, Watts C. Daily prognostic estimates for critically ill adults in intensive care units: results from a prospective, multicenter, inception cohort analysis. Crit Care Med 1994;22:1359–72.
26. Johnston JA, Wagner DP, Timmons S, Welsh D, Tsevat J, Render ML. Impact of different measures of comorbid disease on predicted mortality of intensive care unit patients. Med Care 2002;40:929–40.
27. Cho DY, Wang YC, Lee MJ. Comparison of APACHE III, II and the Glasgow Coma Scale for prediction of mortality in a neurosurgical intensive care unit. Clin Intensive Care 1995; 6:9–14.
28. Russell JA, Singer J, Bernard GR, Wheeler A, Fulkerson W, Hudson L et al. Changing pattern of organ dysfunction in early human sepsis is related to mortality. Crit Care Med 2000;28:3405–11.
29. Pompei P, Foreman M, Rudberg MA, Inouye SK, Braund V, Cassel CK. Delirium in hospitalized older persons: outcomes and predictors. J Am Geriatr Soc 1994;42:809–15.
30. Rabins PV, Folstein MF. Delirium and dementia: diagnostic criteria and fatality rates. Br J Psychiatry 1982;140:149–53.
31. McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. Arch Intern Med 2002;162:457–63.
32. Truman B, Ely EW. Monitoring delirium in critically ill patients. Crit Care Nurse 2003;23:25–36.
33. Lawlor PG, Gagnon B, Mancini IL, Pereira JL, Hanson J, Suarez-Almazor ME et al. Occurrence, causes, and outcome of delirium in patients with advanced cancer: a prospective study. Arch Intern Med 2000;160:786–94.
34. Inouye SK, Schlesinger MJ, Lyndon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. Am J Med 1999;106:565–73.
35. Francis J, Kapoor WN. Prognosis after hospital discharge of older medical patients with delirium. J Am Geriatr Soc 1992;40:601–06.
36. Levkoff SE, Evans DA, Liptzin B, Cleary PD, Lipsitz LA, Wetle TT et al. Delirium: the occurrence and persistence of symptoms among elderly hospitalized patients. Arch Intern Med. 1992;152:334–40.
37. Marcantonio ER, Goldman L, Mangione CM, Ludwig LE, Muraca B, Haslauer CM et al. A clinical prediction rule for delirium after elective noncardiac surgery. JAMA 1994; 271:134–9.

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