Delirium in critically ill patients: incidence, risk factors and outcomes

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Abstract

***Objective*: To determine the incidence, and evaluate the risk factors and outcomes of delirium in general Intensive Care Unit (ICU).**

***Design*: Prospective cross-sectional observational study.**

***Setting*: Teaching hospital in Kuala Lumpur, Malaysia.**

***Patients and participants*: Patients ages of 18 and above admitted for more than 24 hours in general ICU were recruited into the study.**

***Measurements and results*:The demographic data, predisposing and precipitating factors, and environmental factors were collected. Confusional Assessment Method (CAM-ICU) was done daily to assess delirium, when the patient had a sedation score of above Richmond Agitation and Sedation Scale (RASS) -3. Patients were followed up till discharged from ICU. Length of mechanical ventilation and length of ICU stay were recorded.**

A total of 139 patients were recruited with overall incidence of delirium was 42%. Among patients who had delirium, 68% were of hypoactive delirium, 25% of mixed delirium and 7% were hyperactive delirium. The significant predisposing risk factors for developing delirium were age, higher Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, visual or hearing impairment, smoking, renal impairment, diabetes, and hypertension. The factors detected precipitating delirium were sepsis, use of vasopressors, renal replacement therapies, and acute respiratory distress syndrome (ARDS). The presence of catheters, higher Sequential Organ Failure Assessment (SOFA) scores, and abnormal urea and bilirubin levels further significantly increased risk of delirium. Environmental conditions increasing the risk of delirium included absence of daylight exposure and visible clocks, and use of physical restraints. As a result of delirium, patients had longer length of mechanical ventilation and ICU stay.

***Conclusions*: Recognizing predisposing factors and optimizing the modifiable risk factors will improve the length of mechanical ventilation and ICU stay.**

Introduction

Delirium in the Intensive Care Unit (ICU) occurs in 60-80% of mechanically ventilated patients and 20-40% of non-ventilated patients. (1,2) Delirium is defined as an acute cognitive impairment accompanied with fluctuating mental status, inattention, and disorganised thoughts. (3) It is characterised by acute to subacute onset of altered consciousness and cognition, frequently with a reduced awareness of the environment, impaired attention, and/or disorganised thinking over a short period of time (hours to days). Incidence of delirium in a study done in Malaysia was found to be around 44%. (4)

Delirium presents as three major subtypes: hyperactive, hypoactive, and mixed, with hypoactive and mixed the most common presentations in critically ill patients. (5,6) Hyperactive delirium is characterised by agitation, restlessness, and attempts to remove tubes and lines. Hypoactive delirium is characterised by withdrawal, flat affects, apathy, lethargy, and decreased responsiveness. Mixed delirium is when patients fluctuate between both types.

Many risk factors exist for the development of ICU delirium. These factors can be delineated into two

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distinct categories: predisposing and precipitating. Predisposing risk factors are often present at ICU admission, are less modifiable, and are a function of patient health status before ICU admission. Predisposing risk factors include advanced age, baseline dementia, depression, injury severity, chronic illness (example: hypertension), visual or hearing impairment and tobacco, alcohol or drug abuse. (7,8) In contrast, precipitating risk factors are those risk factors that are not present at ICU admission and may be the most modifiable. Precipitating factors include medication such as benzodiazepines, dehydration, sepsis, seizures, metabolic disturbances, and head trauma. (7,8)

Confusional Assessment Method Intensive Care Unit (CAM-ICU) (**Appendix A**) and Intensive Care Delirium Screening Checklist (ICDSC) (**Appendix B**) are two validated tools used to assess delirium among mechanically ventilated patients. For this study, CAM-ICU was used because it is the most widely used instrument for diagnosing delirium by intensivists and other non-psychiatrists and has been found to have the best combination of ease, speed, reliability and validity. (2) According to two systematic reviews and meta-analyses, the CAM-ICU's pooled sensitivity was 76% and 80%, respectively, and pooled specificity was 96% in both studies. The pooled sensitivity for the ICDSC was 74% and 80%, and the pooled specificity was 75% and 82%. (9,10)

Delirium is associated with prolonged mechanical ventilation and length of stay, persistent cognitive impairment post hospital discharge, increased likelihood of transfer to chronic care facility, higher costs, and increased mortality. (11-13)

Recognition of delirium and risk factors is therefore crucial to prevent further morbidity and mortality in ICU. Treatment for delirium include pharmacological and non-pharmacological therapy. Pharmacological treatment includes use of antipsychotics such as haloperidol and quetiapine. Non pharmacological treatment include use of the Awakening and Breathing Coordination, Delirium monitoring/management and Early exercise/mobility (ABCDE) bundle. (14)

Materials and methods

Study design

This was a prospective cross sectional observational study on delirium among patients in General ICU Universiti Kebangsaan Malaysia Medical Centre by multiple investigators. Patients above the age of 18 years old with an admission of more than 24 hours in ICU were included into the study. The exclusion criteria were patients with neuropsychiatric disorders, and language difficulty. Informed consent was taken from patients or the next of kin if unfit to give consent themselves.

Delirium assessment

All patients were assessed for the level of sedation using Richmond Agitation and Sedation Scale (RASS) (**Appendix E**). This scale consists of 10 levels. Level of sedation was categorised as deep sedation (RASS -3 to -5), light sedation (RASS -2 to +1) and agitated (RASS +2 to +4). CAM-ICU was scored daily for every patient after morning rounds if a patient had a sedation score of above RASS -3. In CAM-ICU, the patient was initially assessed for altered or fluctuating mental status, as well as inattention using a 10 letter sequence where the patient was required to squeeze the assessors hand only when the letter A is stated. The patient was then assessed for disorganised thinking by their ability to answer four simple yes/no questions and a command for reduced level of consciousness. Patients were defined as delirium if altered mental status and inattention were present with disorganised thinking and/or reduced level of consciousness. The patients were categorised as delirium if CAM-ICU is positive, no delirium if CAM-ICU is negative, and if deeply sedated (RASS -4 to -5) as Unable to Assess (UTA). Patients were then grouped as delirium (Group D) and non-delirium (Group ND).

Assessment of risk factors

Risk factors for the development of delirium is dependent on a complex interplay between predisposing and precipitating risk factors based on the model of Inouye and colleagues. (15)

Predisposing factors

Predisposing factors were obtained from next of kin or patients themselves if able to, or from documented medical notes before illness with regards to baseline mental status, smoking history, alcohol or drug abuse, visual and/or hearing impairment as well as smoking history and preexisting chronic illness. The demographic data such as age, gender, weight, and height were collected. Patients were followed up until discharged from ICU. Acute Physiology and Chronic Health Evaluation II (APACHE II) score on admission (**Appendix C**) and daily Sequential Organ Failure Assessment (SOFA) score were charted (**Appendix D**).

Precipitating factors

As for precipitating factors, data was acquired from documented medical notes and investigation

results, pertaining to sepsis (evidence systemic inflammatory response syndrome [SIRS] and positive blood culture), use of renal replacement therapy, acute respiratory distress syndrome (ARDS) and use of vasopressors or inotropes, and laboratory abnormalities (serum sodium, serum glucose, bilirubin and urea). Type and number of catheters were also noted.

Environmental factors
Lastly environmental factors such as room without windows in isolation, any visible clocks, and immobility (unable to move upper and/or lower limb) was also investigated.

Outcomes
Outcomes of these patients, pertaining length of mechanical ventilation and duration of ICU stay were also investigated.

Statistical analysis
The study was designed with type I error of α=0.05, type II error of β=0.2 and power of 80% with expected incidence of delirium was 40-60% the calculated sample size was 121 patients as including 20% dropout rate. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 22.0 IBM Corp, Armonk, NY) software. The comparison of demographic and clinical continuous variable between delirium and non delirium group was done using student t test or Wilcoxon rank-sum test. Chi-square test or Fisher exact test was used for categorical variables. Univariate and multivariate logistic regression analysis was used to evaluate the association of potential covariates with first delirium event. A p value of <0.05 was considered statistically significant.

Results
A total of 139 patients were enrolled in the study period. Out of this, 59 (42%) were found to have delirium. Out of the patients who had delirium, 40 (68%) were hypoactive delirium, 15 (25%) were of mixed delirium, and 4 patients (7%) were hyperactive delirium. The demographic data are shown in **Table 1**.

Predisposing factors
Predisposing factors that were statistically significant between both groups were age, APACHE II scores, visual or hearing impairment, smoking, renal impairment, diabetes as well as hypertension are shown in **Table 2**.

Precipitating risk factors
Patients with ARDS, vasopressors or inotropes usage, patients requiring renal replacement therapies, and sepsis were the acute illnesses precipitating delirium that were statistically significant between both groups. In terms of laboratory indices, electrolytes, urea, and bilirubin levels between both groups showed a difference, which were statistically significant as to SOFA scores. Patients with dialysis catheters, central venous catheters, and nasogastric tubes were statistically significant to have higher incidence of delirium. Patients with delirium also had statistically significant higher number of catheters. Results are shown in **Table 3** below.

Environmental conditions
Environmental conditions such as no exposure to daylight, no visible clocks, and use of physical restraints showed statistically higher incidences of delirium as seen in **Table 4**.

Multivariate analysis
Following multivariate analysis, two factors showed increased statistical significance. Smoking cigarettes by every ten years increased the risk of developing delirium by a factor of 1.13 (95% CI 1.01-1.27, p=0.04) and every 10 increments of SOFA score, increased the risk by a factor of 4.77 (95% CI 1.76-12.90, p=0.01)

Outcome
The length of ICU stay and length of mechanical ventilation were statistically longer among patients who had delirium with a median of 4 and 3 days respectively and the correlation was significant (r=0.61; p=0.001, r=0.82; p=0.001). The scatter plot is shown in **Figure 1**.

Discussion
The incidence of delirium in our study was similarly reported by Shehabi et al who conducted a study in ICU of government hospitals and 2 teaching hospitals in Malaysia, which detected an incidence of 44%. (4) In contrast, the incidence of delirium observed by Van Rompaey et al (2009) was lower by 12% and Sharma et al (2012) revealed even lower incidence at 24.4%. (16,17) The marked difference seen in the incidences between our study and Van Rompaey et al and Sharma et al possibly could have been attributed to their larger sample sizes, and the different methods used to assess delirium. Van Rompaey et al utilised the Neelon and Champagne Confusion Scale (NEECHAM) and

Sharma et al used the Delirium Rating Scale Revised-98 (DR-SR-98), while like us Shehabi et al utilised CAM-ICU. NEECHAM scale has the advantage that it can detect delirium in the early stages and DR-SR-98 has been validated against dementia and other psychiatric disorders. (18,19) Although CAM-ICU does not allow stratification of delirium according to severity, it is a simple and rapid tool to assess delirium in ICU patients. (2)

Predisposing factors

We found that cigarette smokers had increased risk of developing delirium. DuBois et al (2001) and Van Rompaey et al (2009) found that smoking doubled the risk of developing delirium. (7,16) Nicotine induces neuroadaptive changes in the brain of the chronic smoker. This causes upregulation of true nicotinic acetylcholine receptors, possibly due to nicotine-induced desensitisation. (20) Nicotine increases dopaminergic and acetylcholinergic transmission. Abrupt cessation of smoking may create an imbalance in neurotransmission particularly related to acetylcholine and dopamine, both of which has been hypothetically linked to neurotransmitter hypotheses of delirium. (21)

We found that higher SOFA score by increments of 10 strongly increased risk of delirium. This finding was similar to Angles et al in 2008, which utilised Denver Multiple Organ Failure system to assess organ failure. (22) They showed that the number of organ failure involved positively correlates with the chance of developing delirium. Inflammatory mediators produced during critical illness which leads to organ failure (for example tumour necrosis factor, interleukin-1) initiate a cascade of endothelial damage, thrombin formation and microvascular compromise. (23) Human brain microvessel endothelial cell showed that the inflammatory mediators can cross the blood-brain barrier and increase vascular permeability in the brain and result in changes on electroencephalogram (EEG) similarly seen in septic patients with delirium. (24)

As Van den Boogard et al (2012) and Shi et al (2010), we detected age as a significant risk factor for the development of delirium. (25,26) The effects of ageing on the brain and cognition are widespread and have multiple aetiologies. The neurotransmitters most often discussed with regards to ageing are dopamine and serotonin. Dopamine levels decline by around 10% per decade from early adulthood and have been associated with declines in cognitive and motor performance. (27) Therefore, elderly patients may be at a higher risk of developing delirium. We noted higher APACHE II scores upon admission to ICU also increased the risk of delirium. These findings were also noted in the study by Shi et al in 2010 and Ouimet et al in 2006. (26,28) The higher the APACHE II score upon admission shows that the patient is more ill and more likely to have worse outcomes.

In our study, patients with pre-existing diabetes and hypertension had increased risk of developing delirium. Hypertension has been linked to development of delirium as shown by DuBois et al (2001) and Ouimet et al (2006) where history of hypertension increased risk of development of delirium by two-fold. (7,28) Vascular disease, a feature of hypertension, puts a patient at higher risk for cerebral hypoperfusion and perhaps cerebral cellular hypoxia. Therefore, in combination with compromised blood pressure during acute illness puts them at risk to develop delirium. Furthermore, hypertensive patients also have neuropsychological effects pertaining to memory, attention and abstract reasoning compared to normotensive patients. (29) Diabetic patients may have similar vascular disease; however the association of diabetes and delirium has not been shown in other studies.

The presence of renal impairment also increased the risk of developing delirium. Pisani et al (2007) also found similar findings, where a serum creatinine of more than 2 mg/dl (176.8 micromol/L) increased risk of developing delirium. (30) The kidney is responsible for excretion of waste products and when there is impairment of the function of the kidney, there is likely to be accumulation of waste products, which could be responsible for further compounding risks for the development of delirium. Visual and hearing impairment increased the risk of developing delirium a finding shared by Mc Nicol et al (2003) where 42.4% of patients with visual or hearing impairment developed delirium. (20) The unfamiliar surroundings and the inability to use their senses (vision and/or hearing) to adapt and adjust to the new environment puts them at risk to develop delirium. It is therefore imperative that during history taking these small details such as use of spectacles and hearing aids are checked.

Precipitating factors

In our study, electrolyte abnormalities pertaining to urea and bilirubin was shown to be a risk factor for the development of delirium. Francis et al (1990) and Aldemir M. et al (2001) also found similar findings. (31,32) Aldemir et al reported an odds ratio 4.6 and 8.3 for abnormal urea and bilirubin levels. Aetiology of uremic encephalopathy suggests imbalances of neurotransmitter amino acids within the brain. During the early phase of uremic

encephalopathy, plasma and cerebrospinal fluid determinations indicate that levels of glycine increase and levels of glutamine and gamma-aminobutyric acid (GABA) decrease; additionally, alterations occur in metabolism of dopamine and serotonin in the brain, which may lead to early symptoms (eg, sensorial clouding) and could be linked to delirium. (33)

Environmental factors

The patient's environment in the ICU also increases a patient's risk to develop delirium. In our study, presence of increasing number of catheters showed increased risk for delirium. In a study by Van Rompaey et al (2009) the presence of more infusions increased risk of delirium. (16) Ill patients have multiple catheters inserted into them such as nasogastric tubes, urinary catheters, central venous catheters, dialysis catheters, and others. These catheters were necessary for their care. However, we suggest to review regularly the need for them so they can be removed in hope to reduce the risk.

The absence of a clock and exposure to daylight were also associated with delirium in our study. Presence of daylight in the patients space should be simulated where possible as there is research stating the disturbance of circadian rhythm might cause delirium. (34) The use of physical restraints in patients were also associated with delirium in this study. Thus, indicating that unnecessary use of physical restraints should be avoided in the ICU. In our ICU, physical restrains were applied onto patients when they were endangering themselves by voluntary or involuntary acts. This finding is similar to the study by Van Rompaey et al in 2009. (16) Physical restraints can cause psychological effects as well as increases the risk of a patient to get soft tissue injuries and fractures.

Outcome

In our study, delirium was detected in 48.7% of mechanically ventilated patients and this association was significant as with length of mechanical ventilation, which was longer in the delirium group. A study by Zhang et al in 2014 showed that length of mechanical ventilation was longer in delirious group, which was 6 days vs 1 day in non delirious group. (35) They also found that length of ICU stay was longer in patients who had delirium. These findings are consistent with multiple studies done previously as reported by a recent meta-analyses. (36,37)

Limitations

There are few limitations in our study. An informal sedation score based on RASS is used in our ICU. A formal documentation of the sedation score is not done. These practices may have influenced the study findings as it affects the use of sedative medications such as benzodiazepines, which in turn can affect the development of delirium. This has been shown in two studies by Pandharipande et al in 2006 and 2008, where benzodiazepine class of drugs (lorazepam and midazolam) are risk factors for transitioning to delirium. (8,38) Another study by Skrobik et al in 2013 found contradictory results where they found that the occurrence of delirium was unrelated to midazolam administration. (39) A future study is required to investigate further the effect of the sedation practices in our ICU on delirium and its outcome. Secondly, the once daily scoring of CAM-ICU might have been inadequate to capture the changes that could have occurred to patients throughout the day as sedation may be withheld and restarted at different times. More frequent assessment of delirium during the course of the day could overcome this problems. Lastly, there may be other unmeasured covariates such as sleep deprivation, which can affect the results.

Table 1. Demographic data, values expressed as median (inter-quartile range), numbers and percentage as parenthesis where appropriate

	Group D (n=59)	Group ND (n=80)	p
Height (cm)	160 (160-165)	160 (155.8-165)	0.770
Weight (kg)	60 (55-70)	60 (50-70)	0.700
Gender - Male - Female	 34 (42.0) 25 (43.1)	 47 (58.0) 33 (56.9)	 0.890

Legend: $p<0.05$ statistically significant.

Table 2. Relationship of predisposing patient factors and delirium. Values expressed as median (inter-quartile range), numbers, percentage as parenthesis, odds ratio (OR) and 95% confidence interval (CI)

	Group D (n=59)	Group ND (n=80)	OR	95% CI	p
Age	65 (51-74)	51 (31-61)	1.05	1.03-1.07	0.001*
APACHE II score	30 (25-35)	25 (25-30)	1.12	1.06-1.19	0.001*
Visual or hearing impairment	16 (27.1)	8 (10.0)	3.35	1.32-8.48	0.010*
Smoking	24 (40.7)	19 (23.8)	2.20	1.06-4.57	0.030*
Years of smoking	10 (10-20)	5 (5-7)	1.13	1.04-1.24	0.010*
Diabetes	38 (64.4)	29 (36.3)	3.18	1.58-6.42	0.010*
Hypertension	40 (67.8)	30 (37.5)	3.51	1.73-7.13	0.010*
Renal impairment (creatinine>110 umol/L)	13 (22.0)	3 (3.8)	2.90	1.97-4.27	0.001*
Dementia	1 (1.7)	1 (1.3)	1.36	0.08- 22.33	0.050
Alcohol	5 (8.5)	3 (3.8)	2.38	0.54-10.37	0.250
Chronic obstructive pulmonary disease	5 (8.5)	1 (1.3)	7.31	0.83-64.37	0.070
Cardiovascular disease	10 (16.9)	3 (3.8)	0.38	0.10-1.43	0.150
Chronic liver disease	-	3 (3.8)	1	-	-

Legend: *=$p<0.05$ statistically significant; APACHE II=Acute Physiology and Chronic Health Evaluation II.

Table 3. Comparison of delirium and precipitating factors. Values expressed as median (inter-quartile range), numbers, percentage as parenthesis, odds ratio (OR) and 95% confidence interval (CI)

	Group D (n=59)	Group ND (n=80)	OR	95% CI	p
Acute respiratory distress syndrome	42 (71.0)	35 (43.8)	3.18	1.55-6.5	0.010*
Vasopressors or inotropes	55 (93.2)	32 (40.0)	20.62	6.8-62.53	0.010*
Renal replacement	24 (40.7)	10 (12.5)	4.80	2.07-11.14	0.010*
Sepsis	34 (57.6)	17 (21.3)	5.04	2.39-10.61	0.010*
SOFA score	9 (8-10)	7.3 (6-9)	1.24	1.08-1.43	0.010*
Laboratory indices					
- Urea level	12.6 (8.6-19)	7.5 (5.5-10)	1.12	1.05-1.19	0.010*
- Bilirubin level	7.5 (6.7-8.9)	7 (5-8)	1.54	1.22-1.95	0.010*
- Sodium level	139.5 (137.8-141)	140 (136.9-140)	1.10	0.99-1.22	0.070
- Glucose level	7.2 (6.6-8)	6.5 (5.5-7.4)	1.15	0.97-1.35	0.100
Catheters					
- Central venous	56 (94.9)	38 (47.5)	20.63	5.96-71.41	0.010*
- Dialysis catheter	24 (40.7)	7 (8.8)	7.25	1.96-26.81	0.001*
- Nasogastric tube	58 (98.3)	56 (70.0)	24.86	3.25-18.99	0.010*
- Drains	19 (32.2)	23 (28.8)	1.18	0.57-2.44	0.660
- Chest tube	1 (1.7)	2 (2.5)	0.67	0.06-7.6	0.750
Number of catheters	4 (3-4)	3 (1-2)	2.60	1.75-3.85	0.010*

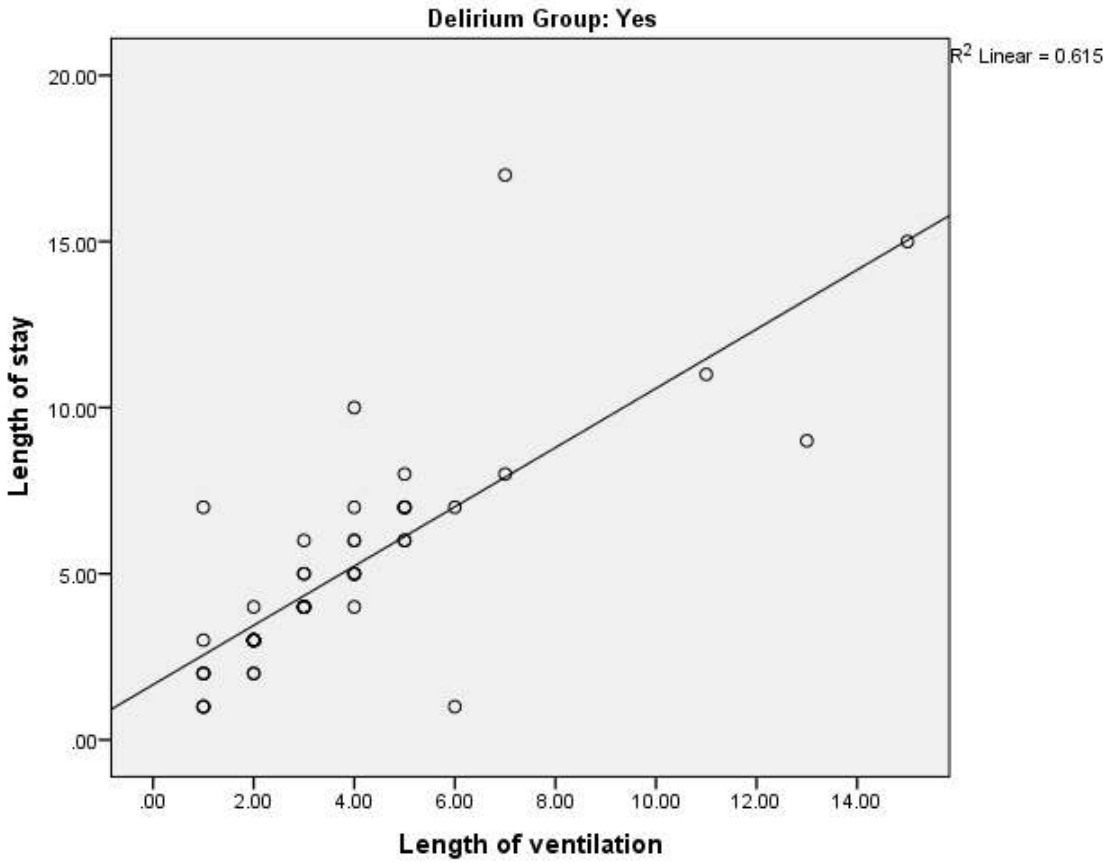
Legend: *=p<0.05 statistically significant; SOFA=Sequential Organ Failure Assessment.

Table 4. Environmental factors and delirium. Values expressed as numbers (n), percentage as parenthesis, odds ratio (OR) and 95% confidence interval (CI)

	Group D (n=59)	Group ND (n=80)	OR	95% CI	p
No daylight exposure	20 (33.9)	10 (12.5)	3.59	1.53-8.43	0.01*
Isolation	6 (10.2)	4 (5)	2.15	0.58-7.99	0.25
No clock visible	40 (67.8)	18 (22.5)	7.25	3.4-15.46	0.01*
Physical restraints	13 (22)	1 (1.3)	22.33	2.83-176.26	0.01*
Immobility	2 (3.4)	1 (1.3)	2.77	0.25-31.31	0.41

Legend: *=p<0.05 statistically significant.

Figure 1. Scatter plot correlation of delirium and length of mechanical ventilation and length of ICU stay



Legend: ICU=Intensive care unit.

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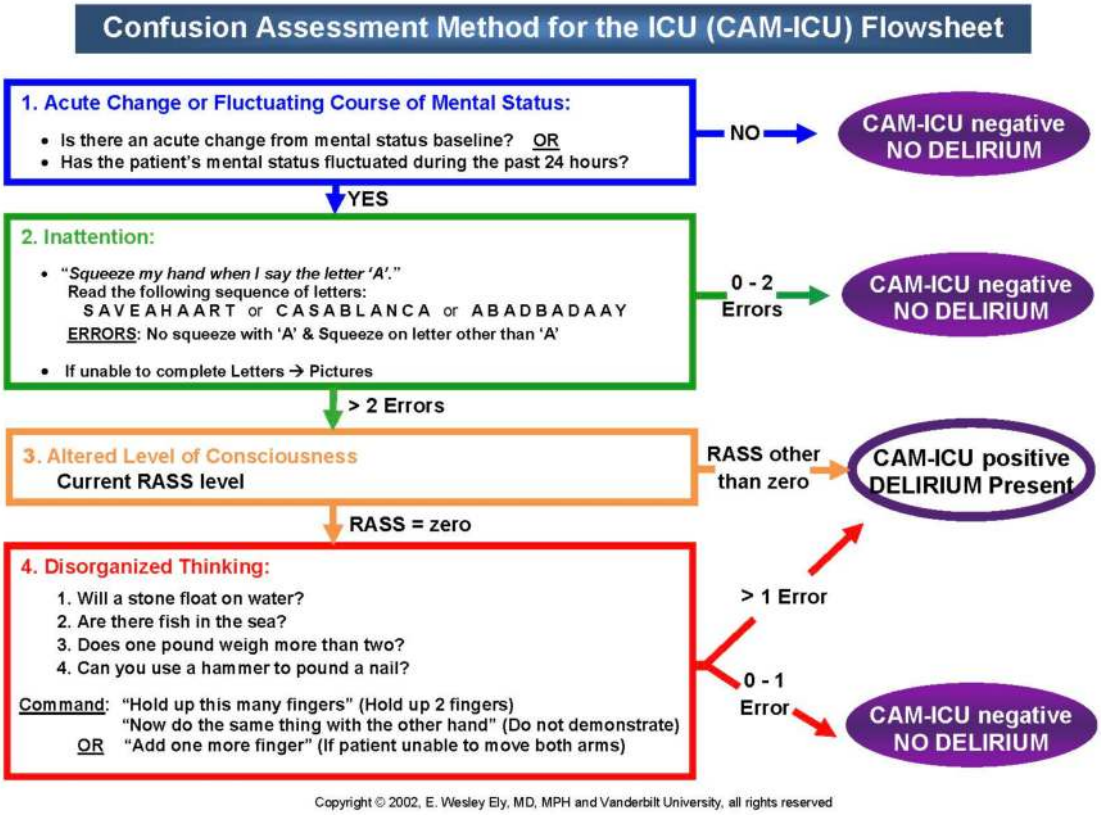
Appendix A. Confusional Assessment Method Flowsheet (adapted with permission from http://www.icudelirium.org/CAM_ICU_trainingmanual_revised_2014.pdf)



CAM-ICU Worksheet

Feature 1: Acute Onset or Fluctuating Course	Score	Check here if Present
Is the patient different than his/her baseline mental status? OR Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e., RASS/SAS), GCS, or previous delirium assessment?	Either question Yes →	☐
Feature 2: Inattention		
Letters Attention Test (See training manual for alternate **Pictures**) Directions: Say to the patient, *"I am going to read you a series of 10 letters. Whenever you hear the letter 'A,' indicate by squeezing my hand."* Read letters from the following letter list in a normal tone 3 seconds apart. **S A V E A H A A R T** or **C A S A B L A N C A** or **A B A D B A D A A Y** **Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A."**	Number of Errors >2 →	☐
Feature 3: Altered Level of Consciousness		
Present if the Actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	☐
Feature 4:Disorganized Thinking		
Yes/No Questions (See training manual for alternate set of questions) 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail? **Errors are counted when the patient incorrectly answers a question.** **Command** Say to patient: "Hold up this many fingers" (Hold 2 fingers in front of patient) "Now do the same thing with the other hand" (Do not repeat number of fingers) *If the patient is unable to move both arms, for 2nd part of command ask patient to "Add one more finger" **An error is counted if patient is unable to complete the entire command.**	Combined number of errors >1→	☐

Overall CAM-ICU **Feature 1 plus 2 and either 3 or 4 present = CAM-ICU positive**		
	Criteria Met →	☐ **CAM-ICU Positive** (Delirium Present)
	Criteria Not Met →	☐ **CAM-ICU Negative** (No Delirium)

Appendix B. Intensive Care Delirium Screening Checklist (ICDSC)

Intensive Care Delirium Screening Checklist (ICDSC)

- Score your patient over the entire shift. Components don't all need to be present at the same time.
- Components #1 through #4 require a focused bedside patient assessment. This cannot be completed when the patient is deeply sedated or comatose (i.e., SAS = 1 or 2; RASS = -4 or -5).
- Components #5 through #8 are based on observations throughout the entire shift. Information from the prior 24 hours (i.e., from prior 1-2 nursing shifts) should be obtained for components #7 and #8.

1. Altered level of consciousness Deep sedation/coma over entire shift [SAS= 1, 2; RASS = -4,-5] = Not assessable Agitation [SAS = 5, 6, or 7; RASS= 1-4] at any point = 1 point Normal wakefulness [SAS = 4; RASS = 0] over the entire shift = 0 points Light sedation [SAS = 3; RASS= -1, -2, -3] = 1 point (if no recent sedatives) = 0 points (if recent sedatives)	No 0	1 Yes
2. Inattention Difficulty following instructions or conversation; easily distracted by external stimuli. Will not reliably squeeze hands to spoken letter "A": S A V E A H A A R T	No 0	1 Yes
3. Disorientation In addition to name, place, and date, does the patient recognize ICU caregivers? Does patient know what kind of place they are in? (List examples such as dentist's office, home, work, hospital.)	No 0	1 Yes
4. Hallucination, delusion, or psychosis Ask the patient if they are having hallucinations or delusions (e.g., trying to catch an object that isn't there). Are they afraid of the people or things around them?	No 0	1 Yes
5. Psychomotor agitation or retardation EITHER: Hyperactivity requiring the use of sedative drugs or restraints to control potentially dangerous behavior (e.g., pulling IV lines out or hitting staff). OR: Hypoactive or clinically noticeable psychomotor slowing or retardation.	No 0	1 Yes
6. Inappropriate speech or mood Patient displays inappropriate emotion, disorganized or incoherent speech, sexual or inappropriate interactions, or is apathetic or overly demanding.	No 0	1 Yes
7. Sleep-wake cycle disturbance EITHER: Frequent awakening/<4 hours sleep at night. OR: Sleeping during much of the day.	No 0	1 Yes
8. Symptom fluctuation Fluctuation of any of the above symptoms over a 24-hour period.	No 0	1 Yes
TOTAL SHIFT SCORE (Min 0 – Max 8)		

Appendix C. APACHE II scoring system

A Acute Physiology Points:

Physiologic variable	High Abnormal Range				Low Abnormal Range				
	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature (rectal, °C)	≥41	39-40.9		38.5-38.9	36- 38.4	34-35.9	32 -33.9	30 -31.9	≤29.9
Mean Arterial Pressure (mm Hg)	≥160	130 – 155	110-129		70-109		50-69		≤49
Heart rate (ventricular response)	≥ 180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory rate (non-ventilated orientation)	≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation: $AaDO_2$ or PaO_2 (mmHg) a. FIO_2 ≥0.5 record only AaDO b. FIO_2 <0.5 record only PaO_2	≥500	350-499	200-349		<200 PO_2 >70	PO_2 61-70		PO_2 55-60	PO_2 <55
Arterial pH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum sodium (mMd/L)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110
Serum potassium (mMd/L)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Serum creatinine (mg/100 mL) (double point score for acute renal failure.)	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White Blood Count	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow Coma Score (GCS) Score = 15 minus actual GCS									
Total Acute Physiology Score									
Serum HCO_3 (venus, mMd/L) (not preferred, use if no ABGs)	≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15

B AGE POINTS:

Assign points to age as follows:

Age (yrs)	Points
≥ 44	0
45 – 54	2
56 – 64	3
65 – 74	5
≤ 75	6

C CHRONIC HEALTH POINTS:

If the patient has a history of severe organ insufficiency or is immunocompromised, assign points as follows:

a. nonoperative or emergency post-operative patients: 5 points

b. elective postoperative patients: 2 points

Definitions: Organ insufficiency or immunocompromised state evident prior to this hospital admission and conforming to the following criteria:
LIVER: Biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma.
CARDIOVASCULAR: New York Heart Association Class IV.
RESPIRATORY: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction, ie, unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mm Hg), or respirator dependency.
RENAL: Receiving chronic dialysis.
IMMUNOCOMPROMISED: Patient has received therapy that suppresses resistance to infection, eg, immunosuppression, chemotherapy, radiation, long term or recent high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection (eg, leukemia, lymphoma, AIDS)

APACHE II SCORE

Sum of A + B + C

A APS Points _____

B Age Points _____

C Chronic Health Points _____

TOTAL APACHE II _____

Legend: APACHE II=Acute Physiology and Chronic Health Evaluation II.

Appendix D. Sequential Organ Failure Assessment (SOFA) scoring

SOFA score	0	1	2	3	4
Respirationa PaO_2/FIO_2 (mm Hg) SaO_2/FIO_2	>400	<400 221–301	<300 142–220	<200 67–141	<100 <67
Coagulation Platelets $10^3/mm^3$	>150	<150	<100	<50	<20
Liver Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular[b] Hypotension	No hypotension	MAP <70	Dopamine </=5 or dobutamine (any)	Dopamine >5 or norepinephrine </=0.1	Dopamine >15 or norepinephrine >0.1
CNS Glasgow Coma Score	15	13–14	10–12	6–9	<6
Renal Creatinine (mg/dL) or urine output (mL/d)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500	>5.0 or <200

Legend: MAP=mean arterial pressure; CNS=central nervous system.

Appendix E. Richmond Agitation and Sedation Scale (RASS)

Richmond Agitation and Sedation Scale

Scale	Description	Definition
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behaviour toward staff
+2	Agitated	Frequent non purposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact to voice ie Eye contact > 10 seconds with verbal stimulation
-2	Light sedation	Briefly (less than 10 seconds) awakening with eye contact to voice ie Eye contact < 10 seconds with verbal stimulation
-3	Moderate sedation	Any movement but no eye contact to verbal stimulation
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation