Risk factors associated with intensive care delirium: a systematic review

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SUMMARY

- Delirium is a neurocognitive disorder characterized by disturbances in consciousness, attention, cognition, and/or perception that develops over a short period and fluctuates over time. Often unrecognized and underdiagnosed, delirium affects a significant portion of the ICU population and is associated with increased length of hospital stay, higher mortality rates, more long-term cognitive deficits, and costlier hospitalizations. The factors contributing to delirium among ICU patients remain poorly understood.
- The objective of this systematized review is to summarize and synthesize the published research literature on risk factors associated with ICU delirium.
- Electronic searches of Cumulative Index of Nursing and Allied Health Literature, MEDLINE, Embase, PsychINFO, and Web of Science were conducted using the Medical Subject Heading "delirium" in various combinations with "intensive care", "critical care", "risk factors", "patient characteristics", "predisposing" and/or "precipitating". Articles were retained if they reported original research involving ICU patients ≥ 18 years of age; were published in English between 2006 and 2014; (iii) focused on risk factors associated with delirium; and used a valid tool for detecting delirium. Quality appraisal was performed using the Newcastle-Ottawa Quality Assessment Scale.
- Twenty-two studies were included in the full review. Delirium is associated with both predisposing factors (patient characteristics and chronic pathologies) and precipitating factors (environmental factors, acute illness, medications, and biochemical markers).
- Conclusions: These results provide an essential step toward identifying factors associated with ICU delirium and may inform the development and testing of delirium risk management guidelines, tools, and protocols to improve client care outcomes.

INTRODUCTION

Delirium is a concern among intensive care unit (ICU) patients (Fong et al., 2009; Maniou, 2012) and their care providers. The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM 5; American Psychiatric Association, 2013) defines delirium as a neurocognitive disorder characterized by disturbances in consciousness, attention, cognition, and/or perception that develops over a short period and fluctuates over time. According to Brummel and Giard (2013), delirium affects a significant proportion of the ICU population, including 20% to 50% of non-mechanically ventilated patients and 60% to 80% of mechanically ventilated patients. Delirium presents in various ways and consequently is often unrecognized and underdiagnosed (Fong et al., 2009; Olson, 2012). It is associated with increased length of hospital stay, higher mortality rates, more long-term cognitive deficits, and costlier hospitalizations (Pun & Boehm, 2011; Skrobik, 2009).

OBJECTIVES

Despite increased delirium research over the past decade, the multiple mechanistic factors that contribute to delirium among ICU patients remain poorly understood. Addressing this knowledge gap is the first step toward raising awareness of risk factors related to ICU delirium; improved patient outcomes through early identification and treatment; and decreasing the burden of this costly complication of acute illness. The objective of this systematized review is to synthesize and summarize the published research literature on risk factors associated with ICU delirium.

METHODS

Electronic searches of Cumulative Index of Nursing and Allied Health Literature (CINAHL), MEDLINE, Embase, PsychINFO, and Web of Science were conducted using the Medical Subject Heading (MeSH) "delirium" in various combinations with the following search terms: "intensive care", "critical care", "risk factors", "patient characteristics", "predisposing" and/or "precipitating". In addition, ancestry searches of reference lists were also conducted to identify relevant articles.

Inclusion/exclusion criteria

Articles were retained for review based on their potential to meet the following inclusion criteria: (i) reports of original research involving ICU patients ≥ 18 years of age; (ii) published in the English language between 2006 and 2014; (iii) focused on a minimum of one risk factor associated with delirium; and (iv) used a valid diagnostic tool for the detection of delirium.

Data extraction

The following data were extracted from each article retained for full review: first author's last name, year of publication, study design, sample size and characteristics, incidence of delirium incidence, delirium assessment tool, frequency of delirium assessment, and the

main significant findings for delirium risk factors (see Table 1). The risk factors were included in Table 1 if they were shown to make made a significant contribution to the development of delirium in univariate or multivariate analyses ($p \leq 0.05$). Data on known risk factors were then grouped into the reference categories of predisposing risk factors or precipitating risk factors, to examine relationships and/or disparities.

Quality appraisal

Quality of each article was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOQAS) (Wells et al., 2000), which is a validated assessment tool for the appraisal of cohort studies. The NOQAS criteria are based on a star system within three domains: (i) selection of cohort (three items); (ii) comparability of the cohorts (two items); and (iii) assessment of outcome (two items). Studies were awarded one star per item in the cohort selection and assessment of outcome domains and a maximum of two stars for comparability. Studies were graded on an ordinal star scoring scale. Studies with seven to nine points were considered of high quality, studies with five to six points were considered of moderate quality, and studies with zero to four points were considered of poor quality.

RESULTS

Search results

The preliminary search yielded 1,281 articles. After duplicates were removed, the titles and abstracts were reviewed to determine if they met the inclusion criteria. One hundred and four articles were further evaluated and 82 were discarded; the remaining 22 articles were included in the full review (Fig. 1).

Study characteristics

All studies 22 studies in the review were published between 2006 and 2014 and involved adult patients in medical, surgical, trauma, burns, cardiac, anesthesiology, respiratory, and general ICUs. All studies provided adequate descriptions of their study population profiles and excluded individuals with such features as aphasia, non-English speaking, or admission of less than 24 hours. Sample size of individual studies ranged from 69-1613 ICU patients. Reported incidence of delirium ranged from 20% to 83%. Twenty of the studies employed a prospective cohort design and used consecutive enrollment to minimize bias; however, only one of these study reported blinding (Pisani et al., 2007). Two studies used chart reviews as their method of data collection (Heymann et al., 2007; Seaman et al., 2006).

Studies differed in the instruments they used to detect and measure delirium; how they measured the risk factors associated with delirium onset; and which factors were measured. The Confusion Assessment Method-ICU (CAM-ICU) was the most commonly used instrument for detecting delirium (18/22 of the studies). Five studies used such other tools as the Delirium Detection Score (DDS), which is used for diagnosis of hyperactive states of delirium only (Heymann et al., 2007); the Intensive Care Delirium Screening Checklist (ICDSC) (Ouimet et al., 2007); the Confusion Assessment Method (CAM) (Seaman et al., 2006); the DSM-IV diagnostic criteria (Sharma et al., 2012); and the Neelon and Champagne Confusion Scale (NEECHAM) (Van den Boogaard et al., 2011). All of the studies commented on validation of the screening tool used; however sensitivity and specificity of the detection tool were reported only in studies that used the CAM or CAM-ICU assessment tool. Most studies assessed patients for delirium once daily using an assessment tool; three studies assessed patients for delirium three times daily (Heymann et al., 2007; Van den Boogaard et al., 2011; Zhang et al., 2014); and two studies reported assessments every one - eight hours and every 12 hours, respectively (Ouimet et al., 2007; Peterson et al., 2006).

Delirium onset was the dependent variable in all of the studies included in the review and all reported the strength of association between delirium onset and various risk factors via odds ratio, relative risk, confidence intervals, or difference of means. Factors were considered to have an association with delirium onset if the observed p-value was ≤0.05. Two studies used solely univariate analysis (Seaman et al., 2006; Sharma et al., 2012) and were evaluated as being of low or moderate quality. The other 20 studies reported using both univariate and multivariate, bivariate or multivariate analyses to identify the relationships among multiple factors and delirium. Of these studies, thirteen were given NOQA scores of 6 (moderate quality) and seven were scored on the NOQA scale as 7 or 8, indicating high quality (Wells et al., 2000).

Predisposing factors

Predisposing factors are influences or patient characteristics that are less likely to be modifiable in reducing the incidence of delirium. Predisposing factors examined in this review can be categorized into two main groups, patient characteristics and chronic health conditions (Table 1)

Patient characteristics

Eleven studies reported increasing age as a potential risk factor for delirium in ICU patients. Lahariya et al. (2014) along with Sharma et al. (2012) reported that with every 1-year increase in age increased the risk of delirium and patients >65 are at greatest risk. Alcohol use was found to be associated with delirium in four studies. Ouimet and colleagues (2007) and Van Rompaey and colleagues (2009) found current tobacco use increased the risk of delirium by a factor of 3.2. An American study that included demographic data on race [White (82%), Black (17%) and other (1%)] found that Black patients had an increased risk of hypoactive delirium (OR = 2.4) (Peterson et al., 2006). A study by Zhang et al. (2014) found patients who lived at home prior to admission were also at an increased risk for delirium.

Chronic health conditions

Studies that examined the association between diabetes mellitus and risk for delirium produced equivocal results, with one showing a strong relationship within their multivariate model (Lahariya et al., 2014) and the other showing a strong relationship with univariate analysis that was lost with multivariate analyses (Lin et al., 2008). Patients with pre-existing congestive heart failure and those with a left ventricular ejection fracture of <30% were found to be at greater risk for delirium, with an OR of 4.06 and 8.21 respectively (Lahariya et al. 2014). Current or past depression also increased the risk for delirium (Lahariya et al., 2014; Pisani et al., 2007). The same authors along with Van Rompaey et al. (2009) found that the presence of a cognitive deficit, cognitive impairment, or dementia also increased the risk for delirium, with ORs of 10.81, 2.41, and 6.3 respectively in multivariate analyses. However, many studies considered cognitive problems as exclusion criteria because alterations in cognitive function can be confused with delirium.

Precipitating factors

Precipitating factors are those risk factors that are potentially modifiable and if a specific targeted interventions are successful, they can reduce the risk of developing delirium. Although a large number of precipitating factors were examined in studies included in this review, most can be grouped into acuity, medications, and biochemical disturbances (see Table 1).

Table 1. Description and summary of studies included in the review. *Only statistically significant results ($p < 0.05$) reported in the Findings column.

Author & publication year	Study design	Setting	Sample size	Delirium assessment tool	Delirium assessment frequency	*Findings specific to delirium risk factors	NOQAS score
Agarwal et al. 2010	Prospective	Burns ICU	Screened: 198; enrolled: 82. Delirium present: 63 (77%)	CAM-ICU	Daily	Benzodiazepine use	6
Angles et al. 2008	Prospective	Trauma ICU	Screened: 102; enrolled: 69. Delirium present: 41 (59%)	CAM-ICU or validated chart review	Daily	Age (per year); ISS; Lower GSC on arrival, number of units of blood transfusions; maximum MOF score	6
Girard et al. 2012	Prospective	Medical ICU	Screened: not indicated; enrolled: 138. Delirium present: 107 (78%)	CAM-ICU	Daily	Lower plasma concentrations of MMP-9 & Protein C. Higher plasma concentrations of sTNFR1	6
Heymann et al. 2007	Retrospective	Anaesthesia ICU or IMCU	Screened: 374; enrolled: 196. Delirium present: 55 (28%). Only screened for hyperactive delirium	Delirium detection score (DDS)	x3 daily	Hyperglycemia; alcohol use; APACHE II score; HAP/VAP; polytrauma; SOFA	6
Lahariya et al. 2014	Prospective	Cardiac ICU	Screened: 321; enrolled: 309. Delirium present: 81 (26%)	CAM-ICU & psychiatric assessment with DSM-IV-TR criteria	Daily	Age (per year); age > 65. Presence of diabetes mellitus. Uncontrolled diabetes mellitus. Congestive cardiac failure. Currently in cardiogenic shock. Undergone cardiac interventions: CABG & angioplasty; LVEF < 30%; current atrial fibrillation; ongoing depression; cognitive deficit (IQCODE); benzodiazepine, opioid, furosemide; warfarin, ranitidine, steroids or non-steroidal anti-inflammatory drugs; > 3 medications; total number of medications; evidence of acute infection; hyponatremia (< 130 mmol/L); hypokalemia (< 3.5 mmol/L); increased creatinine levels (>1.2mg/dl); anemia; hypoglycemia (3.9 mmol/L). APACHE-II Score, SOFA score; Charlson score	6
Lat et al. 2009	Prospective	Surgical ICU	Screened: 665; enrolled: 134. Delirium present: 84 (63%)	CAM-ICU	Daily	Cumulative: lorazepam dose & fentanyl dose; APACHE II score	7
Lin et al. 2008	Prospective	Medical ICU	Screened: 175; enrolled: 143. Delirium present: 31 (22%)	CAM-ICU	Daily for first 5 days	Diabetes mellitus, sepsis, hypoalbuminemia	8
McPherson et al. 2013	Prospective	Cardiac ICU	Screened: 282; enrolled: 200. Delirium present: 53 (27%)	CAM-ICU	Daily for 10 days (max)	Benzodiazepine use on admission (first 24/hours) or daily; physical restraints; age	7
Ouimet et al. 2007	Prospective	Medical/ surgical ICU	Screened: 820; enrolled: 764. Delirium present: 243 (32%)	ICDSC	1-8 hourly verified by physician	Current tobacco consumption; alcohol use; hypertension; APACHE II score; sedative & analgesics used to induce coma; epidural catheter use; average opiate dose; average benzodiazepine dose; average propofol dose; average indomethacin dose; coma (all types); pain	7
Pandharipande et al. 2006	Prospective	Mixed ICU	Screened: 275; enrolled: 198. Delirium present: total number not indicated	CAM-ICU	Daily	Lorazepam use; age (per year); APACHE II score	6
Pandharipande et al. 2008	Prospective	Surgical ICU & trauma ICU	Screened: 142; enrolled: 97. Delirium present: 68 (70%)	CAM-ICU	Daily for 10 days (max)	Midazolam; fentanyl (SICU patients only)	6
Pandharipande et al. 2009	Prospective	Mixed ICU – medical/ surgical	Screened: 103; enrolled: 97. Delirium present: not indicated	CAM-ICU	Daily	Plasma tryptophan/LNAA ratio; age; APACHE II score; fentanyl use; tyrosine/LNAA ratio	6
Peterson et al. 2006	Prospective	Medical ICU	Screened: 824; enrolled: 614. Delirium present: 225 (37%)	CAM-ICU	12 hourly	Age (> 65 years): in association with hypoactive delirium; mechanical ventilation: in hypoactive & mixed-type delirium; APACHE II score: in hypoactive & mixed-type delirium; Black race; hypnotic meds; opiate or neuroleptic medications	6
Pisani et al. 2007	Prospective	Medical ICU	Screened: 725; enrolled: 304. Delirium present: 214 (70%)	CAM-ICU	Daily	Depression; APACHE II score, dementia; benzodiazepine use before admission; elevated creatinine level; low arterial pH; low sodium or potassium on admission; high WBC count on admission; high ALT or AST on admission	8
Schreiber et al. 2014	Prospective	Multiple ICUs	Screened: 520; Enrolled: 330. Delirium present: (83%)	CAM-ICU	Daily	Older age (40–60 years); age ≥ 60 years; systemic corticosteroids; opioid use before admission; SOFA score	6
Seaman et al. 2006	Retrospective	General ICU	Screened: 126; enrolled: 101. Delirium present: 30 (30%)	CAM	Retrospective	Age; oxygenation: hemoglobin, hematocrit; pulse oximetry data; oxidative stress: sepsis or pneumonia	4
Sharma et al. 2012	Prospective	Respiratory ICU	Screened: 140; enrolled: 140. 34 (24%) at 24 hours; 75 (54%) total over ICU stay	DSM-IV	Daily	Age (per year); age (>65years); Glasgow Coma Scale score; APACHE II score; hyperuricemia; hypoalbuminemia; acidosis; abnormal ALT levels; mechanical ventilation; higher number of total medication received; use of sedatives, steroids & insulin	6
Tsuruta et al. 2010	Prospective	Trauma ICU	Screened: 172; enrolled: 103. Delirium present: 21 (20%)	CAM-ICU	Daily	Use of sedatives; APACHE II score; mechanical ventilation; serum max-CRP	6
Van den Boogaard et al. 2011	Prospective	Medical/ surgical ICU	Screened: 105; enrolled: 100. Delirium present: 50 (50%)	CAM-ICU	x3 daily	IL-8 in inflamed patients; IL-10 in non-inflamed patients; Ab1-42/40 in non-inflamed patients	7
Van den Boogaard et al. 2012	Prospective	General ICU	Screened: 2116; enrolled: 1613. Delirium present: 411 (26%)	CAM-ICU	Daily	Age (in years); APACHE-II score; coma: drug induced, other sources or combination; admission category: medical, trauma, or neurology/ neurosurgery; infection; metabolic acidosis; morphine dosing; use of sedation; urea (mmol/L); urgent admission	8
Van Rompaey et al. 2009	Prospective	Multiple ICUs	Screened: number not indicated; enrolled: 523. Delirium present: 155 (30%)	NEECHAM Confusion Scale	Not indicated	> 3 units of alcohol/day; number of cigarettes/day; > 10 cigarettes/day; predisposing cognitive impairment; benzodiazepine or other sedative use; high mortality risk; SAPS II score; high TISS 28 score; ET-tube or tracheostomy; gastric tube; bladder catheter; > 3 perfusions; isolation; no visible daylight; no visitors; physical restraints.	6
Zhang et al. 2014	Prospective	Mixed ICU	Screened: number not indicated; enrolled: 223. Delirium present: 54 (24%)	CAM-ICU	x3 daily	Elevated CRP; APACHE II score; age (in years); CPB surgery; neurological condition; tracheal intubation; living alone; physical restraints; prior alcohol use; mechanical ventilation	6

LEGEND: NOQAS, Newcastle-Ottawa Quality Assessment Scale; OR, odds ratio; CI, confidence interval; sTNFR1, soluable tumor necrosis factor receptor-1; IMCU, intermediate care unit; APACHE, Acute Physiology and Chronic Health Evaluation; HAP/VAP, hospital/ventilator-acquired pneumonia; SOFA, Sequential Organ Failure Assessment; DSM IV-TR, Diagnostic and Statistical Manual for Mental Disorders, 4th edition -Text Revision; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; ICDSC, Intensive Care Delirium Screening Checklist; LNAA, large neutral amino acid; WBC, while blood cell; ALT, alanine aminotransferase; AST, aspartate aminotransferase; IL, interleukin; Ab1, albumin; NEECHAM, Neelon and Champagne Confusion Scale; SAPS, Simplified Acute Physiology Score; ET, endotracheal; CRP, C-reactive protein.

Acuity of illness

The Acute Physiology and Chronic Health Evaluation (APACHE II) score is an indicator of severity of illness and is performed within 24 hours of patients' admission to an ICU (Knaus et al., 1985). An integer score from 0 to 71 is computed based on several measurements; scores ≥ 24 are associated with more severe disease and a higher risk of death (Knaus et al., 1985). Ten studies found a significant association between higher baseline APACHE II scores and delirium. For example, Van Rompaey et al. (2009) reported that patients with a baseline APACHE II score of ≥ than 24 were 2.5 times more likely to develop delirium.

Other scoring systems assessing illness/disease severity or related acuity indices (mortality risk, organ failure, treatment-related activities and the associated nursing workload, and level of consciousness) have been used to assess the relationship between delirium and multiple specific factors. Mechanical ventilation was found to have an association with delirium in four studies (Peterson et al., 2006; Sharma et al., 2012; Tsuruta et al., 2010; Zhang et al., 2014); however other studies excluded patients requiring mechanical ventilation and heavy sedation because the diagnosis of delirium may not be appropriate in those populations.

The presence of acute illness (e.g., pneumonia, cardiogenic shock, infection, new onset of atrial fibrillation, sepsis, requiring blood transfusion, and hypertension) was associated with delirium, with ORs ranging from 3.65 to 10.61 (Angles et al., 2008; Heymann et al., 2007; Lahariya et al., 2014; Lin et al., 2008; Ouimet et al., 2007; Seaman et al., 2006; Van den Boogaard et al., 2011). Patients who required invasive interventions such as cardiopulmonary bypass, angioplasty, or coronary artery bypass grafting (Lahariya et al., 2014; Zhang et al., 2014), those admitted with polytrauma (Heymann et al., 2007; Van den Boogaard et al., 2012; Zhang et al., 2014) and those with multiple drains, tubes, and catheters (Van Rompaey et al., 2009) have all been showed to be at an increased risk for delirium.

Medications

The most frequently studied drugs included opioids, benzodiazepines, and other sedatives. Benzodiazepines and other sedative agents were consistently shown to increase the risk of developing delirium. Opioids were also associated with delirium in seven studies, with ORs ranging from 1.2 to 8.85, depending on the average daily dose administered. However, Pisani et al. (2007) and Van Rompaey et al. (2009) found no statistical link between the use of opioids and delirium onset. In a study specifically looking at Fentanyl in a group of surgical and trauma ICU patients, only the surgical patients had higher likelihood of developing delirium (OR 3.99) (Pandharipande et al., 2009). The authors of the study did not control for dosing levels, making interpretation of the results difficult. Other medications found to increase the risk of delirium included: furosemide, warfarin, ranitidine (Lahariya et al, 2014), steroids (Lahariya et al, 2014; Sharma et al., 2012; Schreiber et al., 2014.) and non-steroidal anti-inflammatories (Lahariya et al, 2014). Multi-drug regimens were also found to be a risk factor for delirium (Lahariya et al. 2014; Sharma et al. 2012).

Biochemical markers

Associations among various metabolic disturbances and delirium have been reported in many of the reviewed studies. Girard et al. (2012) studied the association of inflammation and coagulation with delirium and found two markers of inflammation [lower plasma concentrations of matrix metalloproteinase-9 (MMP-9) and protein C] and one marker of coagulation [higher concentrations of soluble tumor necrosis factor receptor-1 (sTNFR1)] that were significantly associated with delirium. Other markers of inflammation and altered coagulation, such as C-reactive protein, myeloperoxidase, neutrophil gelatinase-associated lipocalin, D-dimer, plasminogen activator inhibitor type 1, and Von Willebrand factor antigen were not associated with delirium. However, both Tsuruta et al. (2010) and Zhang et al. (2014) reported a significant relationship between levels of C- reactive protein and delirium. Alterations in blood glucose levels have also been examined as risk factors for delirium, with a positive association found for hyperglycemia (Heymann et al. 2007), but not for hypoglycemia (Lahariya et al. 2014). The relationship between blood glucose levels and delirium is further complicated when insulin is used as a component of treatment, as insulin has also been shown to be an independent risk factor for delirium (Sharma et al., 2012).

Blood sampling across many studies have revealed multiple alterations that increase the risk of delirium, including low arterial pH, metabolic acidosis, high levels of urea and creatinine, hyponatremia, hypokalemia (Sharma et al., 2012; Van den Boogaard et al., 2012; Lahariya et al. 2014; Pisani et al. 2007). Other markers observed to have an association with delirium include: anemia (Lahariya et al., 2014), hypoalbuminemia (Lin et al., 2008; Sharma et al., 2012), elevated white blood cell count (WBC) (Pisani et al., 2007), high alanine transaminase (ALT) (Pisani et al., 2007; Sharma et al., 2012), high aspartate aminotransferase (AST) (Pisani et al., 2007) , and shifts in plasma tryptophan/LNAA ratio, and tyrosine/LNAA ratio (Pandharipande et al., 2009).

Environmental factors were the focus of a small number of studies. Significant relationships were found with delirium and the use of physical restraints, isolation within the ICU, lack of exposure to sunlight, and having no visitors (McPherson et al., 2013; Van Rompaey et al., 2009; Zhang et al., 2014).

DISCUSSION

Findings from 22 research papers, including 20 prospective cohort studies and two retrospective chart analyses were included in this systematized review, revealed a multiplicity of factors that have been examined and found to be associated with increased risk for developing delirium during a stay in an ICU. These factors were categorized as either predisposing factors (patient characteristics and chronic health conditions) or precipitating factors (environmental factors, acute illness, medications, and biochemical markers) that are associated with ICU delirium.

Despite the apparent numerous factors contributing to ICU delirium, the extent of which this knowledge is known to ICU care providers and strategies to attenuate delirium risk are incorporated into standards of care is unclear. Recognizing these factors and creating clinical screening tools that assess those that most influence the onset of delirium is crucial. Age, dementia, severity of disease, medications, and biochemical changes have all been outlined as strong causative factors for ICU delirium.

Age has consistently been shown to be a statistically and clinically significant risk factor for delirium in half of the studies included in this review (Table. 1), with age > 65 being the most consistent finding. A history of cognitive dysfunction was also found to be an important risk factor in association with delirium. Future studies are needed to explore possible strategies of delirium prevention including specific approaches for the detection of patients with dementia and the differentiation of delirium from dementia. Screening newly admitted patients with a dementia-screening instrument to detect those who are vulnerable could be beneficial in the adult ICU population. It is possible to target those patients with dementia with reorientation strategies that have demonstrated to be effective for delirium prevention (Skrobik, 2009).

Severity of disease, measured by the APACHE II score and other scoring systems presents as an important factor for clinicians to consider in practice. Perhaps risk management guidelines for delirium should include routine and ongoing assessment of

acuity as a component of a delirium detection screening protocol. The use of opioids, benzodiazepines, and other sedative agents were also identified as major contributors to the development of delirium. Continuous assessment of patient need for sedative or analgesic medications may allow for reduction or decreased dose of these drugs. Further clinical trials are needed to analyzing whether alternative management strategies, specific choices of sedative and analgesic agents or multi-modal approaches that combine pharmacological and non-pharmacological strategies are associated with reductions in delirium. Promising studies of such non-pharmacological approaches include the use of guided imagery, therapeutic massage and ear phones delivering music (Hu et al. 2015; Casida & Lemanski, 2010). Many of the biochemical changes that were associated with delirium are common occurrences in ICU patients and are indicative of specific organ or multi-organ dysfunction. Timely therapeutic responses to such physiological alterations are important opportunities to limit the risk of delirium.

CONCLUSIONS

In summary, a large number of predisposing and precipitating factors increase the risk of developing delirium in ICU patients. In addition to the many that have been identified, the potential for the synergistic and/or additive impact of multiple factors occurring at the same time has not been fully explored. This needs to be the focus of further research efforts. This review provides an essential step to identifying at risk patients and understanding the heterogeneity of factors associated with onset of delirium. These results can help guide the development and testing of clinically relevant delirium risk management guidelines, tools and protocols that can be easily incorporated into standards of care. Delirium can be a serious consequence of a ICU admission, costly to the health care system and to individuals who experience delirium. Some of the identified risks are modifiable. Decreases in the incidence and severity of ICU delirium should be considered essential areas of quality improvement for ICU care providers and hospital administration.

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