ICU Delirium Viewed Through the Lens of the PAD Guidelines and the ABCDEF Implementation Bundle

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Objectives

- Outline the salient clinical relevance of delirium to the course and outcome of patients suffering from potentially life-threatening critical illness
- Review the most recent guidelines from the Society of Critical Care Medicine for elements of pain, agitation, and delirium within the construct of a clinical discussion
- Outline the evidence-based ABCDEF bundle with a focus on delirium

Key words: delirium, dementia, sedation, pain, protocol, bundle, critical care, ICU rehabilitation, clinical outcomes, ICU

Medicine has as its means diagnosing, curing, and saving lives toward the end goal of preserving and improving health, self-worth, and personal dignity. Do not confuse the "means" with the "end." To accomplish the means at the expense of the end is to fail.

— Irwin Cohen, Tulane Medical School, 1989

This quotation speaks to the fact that we must be careful that the means of diagnosing, curing, and saving lives in our ICUs don't result in sacrificing our ultimate goal as healthcare professionals, which is stated clearly above as preserving and improving health, self-worth, and personal dignity. We have learned over the past 1 to 2 decades that there are many things we can do that result in survival, yet a sort of "dehumanizing" survival that sacrifices our patients' quality of life and well-being. This chapter presents a clinically based discussion that follows the pain, agitation, and delirium (PAD) guidelines and incorporates an ABCDEF bundled approach to care to help us adjust the "means" to accomplish the "goals" for each and every patient.

CLINICAL CASE

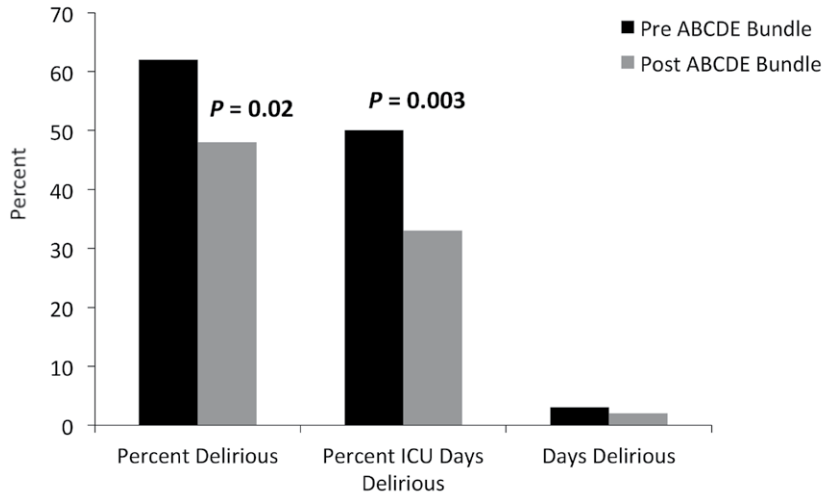
A 54-year-old male with a remote history of resection for gastric carcinoma presented to the emergency department 2 days after gastrojejunal stricture dilation; he had hematemesis, lightheadedness, and diffuse abdominal pain. The patient was admitted to the surgical ICU after an abdominal computed tomography scan, which showed pneumoperitoneum. The cause of his upper gastrointestinal bleeding was thought to be ruptured viscera secondary to the dilation procedure. Initially in the emergency department, his sensorium was clear, his Richmond Agitation-Sedation Scale (RASS) score was 0, and the result of his Confusion Assessment Method in the ICU (CAM-ICU) screening was negative. After the patient was stabilized, he was sent to the operating room, where his perforated abdominal viscera was repaired, and he was then returned to

the ICU with an open abdomen, receiving fentanyl and midazolam infusions to a target RASS of –3. The next morning he was weaned off sedation with a target RASS of 0, yet he was CAM-ICU positive and his actual RASS fluctuated between +2 and –3 (agitation to deep sedation). *What is the best approach to managing this patient's delirium?*

IMPLEMENTATION OF THE PAD GUIDELINES USING THE ABCDEF BUNDLE

The Society of Critical Care Medicine (SCCM) has endorsed and published the 2013 PAD guidelines,[1] which outline the best evidence available for addressing the inextricably linked elements of patient comfort and safety—pain, agitation, and delirium. There is more than one way of changing practice to implement the PAD guidelines, and perhaps the most important thing for a team or individual clinician to acknowledge is that change is indeed needed. We must constantly ask ourselves how we can incorporate new information to better serve our patients. Since humans are reticent to change, many ICUs have found adoption of the PAD guidelines difficult in practice and have had poor compliance with individual steps of quality improvement projects. Because of this repetitive story (ie, initial success but subsequent failure), we have created an evidence-based, bundled approach that your team might consider or draw from as you pursue clinical application of the PAD guidelines. The SCCM is embarking on a PAD implementation program called the ICU Liberation Collaborative, which is framed around a 6-step approach called the ABCDEF bundle[2,3] (Assess, prevent, and manage pain; Both spontaneous awakening trials and spontaneous breathing trials; Choice of sedation and analgesia; Delirium assessment, prevention, and management; Early mobility and exercise; and Family communication and involvement). Balas et al. showed a reduction in the percentage of time ICU patients spent in delirium once the ABCDEs had been implemented (**Figure 1**).[2] After multivariable adjustment for important covariates, that investigation further showed that patients who received the bundle had a 50% reduction in the risk of delirium, 3 fewer days on mechanical ventilation, and double the chance of achieving early mobilization compared with patients who did not receive the bundle.2 From this point onward, we will break the process down into its component parts. All of these aspects are covered in more depth elsewhere in the book, and here we are trying to show how they will be handled globally as a bundle.

Figure 1. *ABCDE delirium results*



Information taken from Balas MC, Vasilevskis EE, Olsen KM, et al. Effectiveness and Safety of the Awakening and Breathing Coordination, Delirium Monitoring/Management, and Early Exercise/Mobility Bundle. *Crit Care Med.* 2014; 42(5):1024-1036.

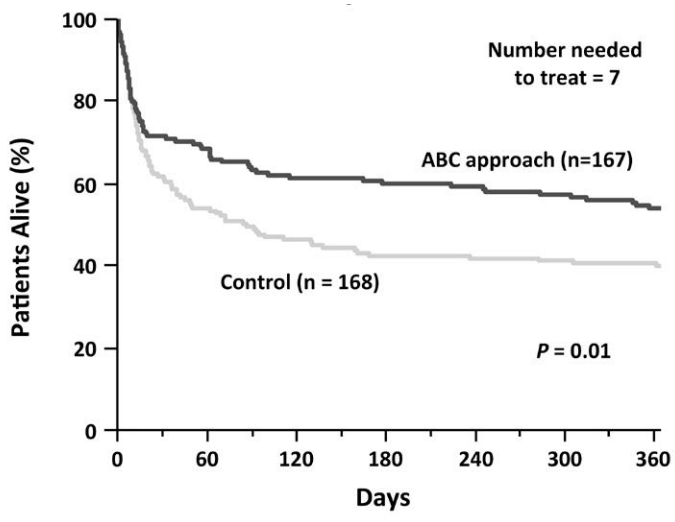
A: Assessment, Prevention, and Management of Pain

Survivors of critical illness testify that pain was an important piece of their suffering while receiving mechanical ventilation, regardless of whether they had other invasive procedures during their ICU stay.[4] Inadequately controlled pain is a risk factor for nosocomial infections and longer durations of mechanical ventilation and may precipitate delirium.[5-7] The PAD guidelines[1] recommend that all adult ICU patients be routinely assessed for pain with an objective, valid, and reliable instrument. Patient self-report is the gold standard for assessment of pain but frequently is impossible while patients are undergoing mechanical ventilation and receiving psychoactive medications.[8] After a thorough psychometric analysis, the Behavioral Pain Scale (BPS)[9] and the Critical Care Pain Observation Tool (CPOT)[10,11] were the only tools recommended by the PAD guidelines[1] for assessing pain in nonverbal ICU patients. The BPS is used to monitor 3 behavioral domains (facial expression, upper limbs, and compliance with mechanical ventilation). The CPOT, the most commonly used of the two instruments, is feasible, easy to complete, and simple to understand and includes evaluation of 4 behaviors (facial expressions, body movements, muscle tension, and compliance with the ventilator for mechanically ventilated patients or vocalization for nonintubated patients). (See "Defining and Implementing the PAD Assessment Tools" chapter for more details on pain assessment.)

B: Both Spontaneous Awakening Trials and Spontaneous Breathing Trials

The next step in ICU liberation is to conduct both a spontaneous awakening trial (SAT) and a spontaneous breathing trial (SBT). This essential component of the modern-day processes of care for all patients receiving mechanical ventilation involves testing each patient who passes the safety screens[12] for his or her ability to tolerate removal of sedatives and narcotics (as long as pain control is achieved) and removal of mechanical ventilation (ie, allowing the patient to experience spontaneous awakening and breathing). The ABC study,[12] also known as the Wake Up and Breathe trial, demonstrated that pairing SATs and SBTs (see "Awakening and Breathing Trials: How To Do Them, What to Do With the Results" chapter for a detailed description) resulted in markedly improved patient outcomes (4 days less in the ICU and hospital and a 14% absolute risk reduction in 1-year mortality) (**Figure 2**). This coordination of SATs and SBTs provides the impetus for excellent teamwork between doctors, nurses, respiratory therapists, pharmacists,

Figure 2. *ABC trial: 1-year survival rate*



Reprinted from Girard TD, Kress JP, Fuchs BD, et al. Efficacy and Safety of a Paired Sedation and Ventilator Weaning Protocol for Mechanically Ventilated Patients in Intensive Care (Awakening and Vreathing Controlled Trial): a Randomized Controlled Trial. *The Lancet*. 371; 126-134. Copyright (2008), with permission from Elsevier.

and others. For every 7 people treated with the Wake Up and Breathe approach, 1 life was saved at 1 year. Furthermore, this emphasizes that sedation cessation plays a pivotal role in patients' abilities to breathe independently and to return to functional and cognitive baseline (see "Ventilating the Awake Patient: Using Other Ventilator Strategies" chapter for more details, including discussion of other investigations informing the literature[2,13,14]).

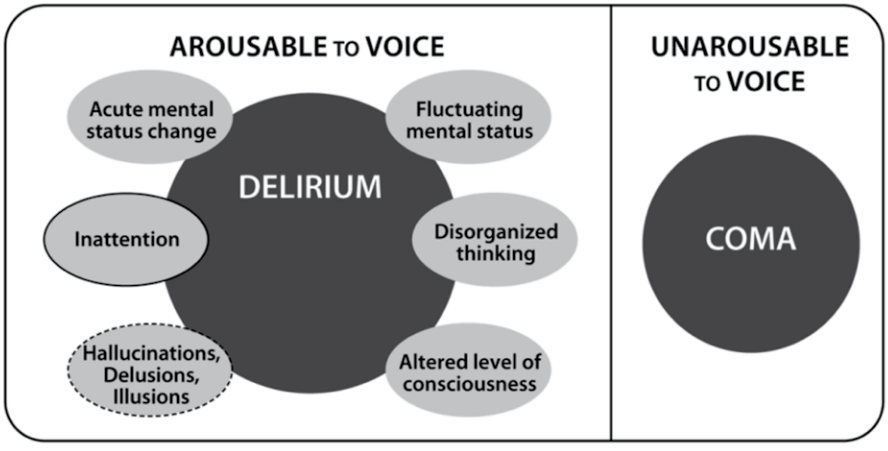
C: Choice of Sedation and Analgesia

Choice of sedation is crucial to patients' clinical outcomes. Psychoactive medication administration should be goal-directed to ensure adequate pain control, anxiolysis, and prevention and treatment of delirium. In addition to selection of drug, the dose, titration, and prompt discontinuation of these medications are of paramount importance. The PAD guidelines[1] recommend that sedative medications be titrated to maintain a light rather than deep level of sedation in adult ICU patients, unless clinically contraindicated. Maintaining light levels of sedation in adult ICU patients is associated with improved clinical outcomes (eg, shorter duration of mechanical ventilation and a shorter ICU length of stay).[15,16] Goal-directed delivery of sedatives is best accomplished by the use of arousal scales, such as the RASS and the Sedation Agitation Scale (SAS) as recommended in the PAD guidelines (see "Defining and Implementing the PAD Assessment Tools" and "Practical Application of a Strategy of Light Sedation for Mechanically Ventilated Patients" chapters). (These are also called sedation scales, but the term *arousal scale* is better since this is part of the routine neurological assessment regardless of whether the patient is receiving sedation.)

D: Delirium Assessment, Prevention, and Management

Delirium is defined in the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) as an acute disturbance of consciousness with inattention accompanied by a change in cognition or perceptual disturbance that fluctuates over time.[17] Three key points to clarifying the syntax surrounding delirium and coma are as follows: First, coma represents the clinical state of a patient who is unarousable to voice (whether this is due to disease or to iatrogenic causes such as deliberate or unintentional overuse of sedation). Second, hallucinations and delusions are not key major components of the diagnosis of delirium. That is, many patients are delirious who do not have either hallucinations or delusions. Third, clinicians need to realize that inattention is the most important diagnostic criterion for delirium (**Figure 3**).[18] Delirium is prevalent,

Figure 3. ***Sedation with propofol is associated with shorter ICU length of stay and improved survival compared with sedation with benzodiazepines***



Reprinted from Morandi A1, Pandharipande P, Trabucchi M, et al. Understanding Iinternational Differences in Terminology for Delirium and Other Types of Acute Brain Dysfunction in Critically Ill Patients. *Intensive Care Med*. 34, 2008, 34 (10)1907-1915. With kind permission from Springer Science and Business Media.

under-recognized, and an independent predictor of poor outcomes such as mortality, prolonged mechanical ventilation, increased length of hospital stay, and long-term cognitive impairment (**Figure 4**).[20,21] Between 50% and 80% of mechanically ventilated ICU patients develop delirium, and this organ dysfunction is missed 75% of the time if not monitored,[23,24] which prompted the PAD guidelines'[1] recommendation that all ICU patients be screened regularly for delirium with a valid and reliable tool. The PAD guidelines

Figure 4. *(a) Dementia following ICU care*

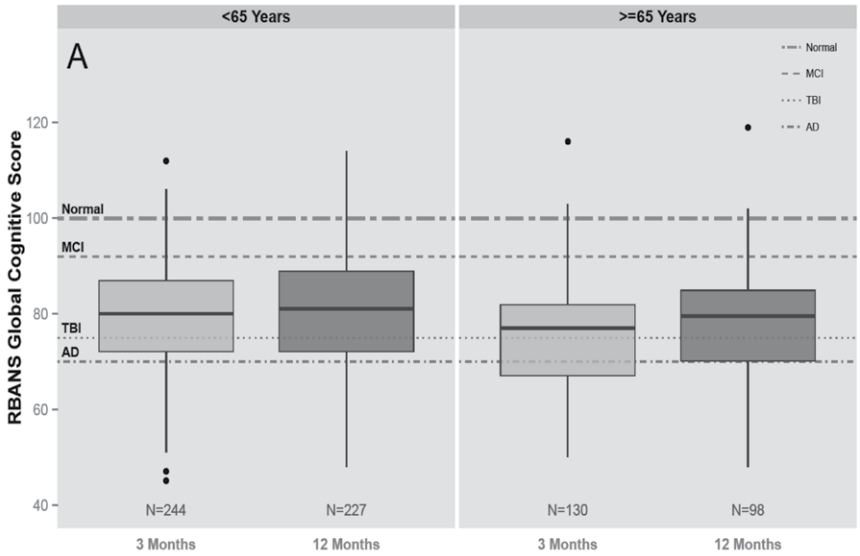
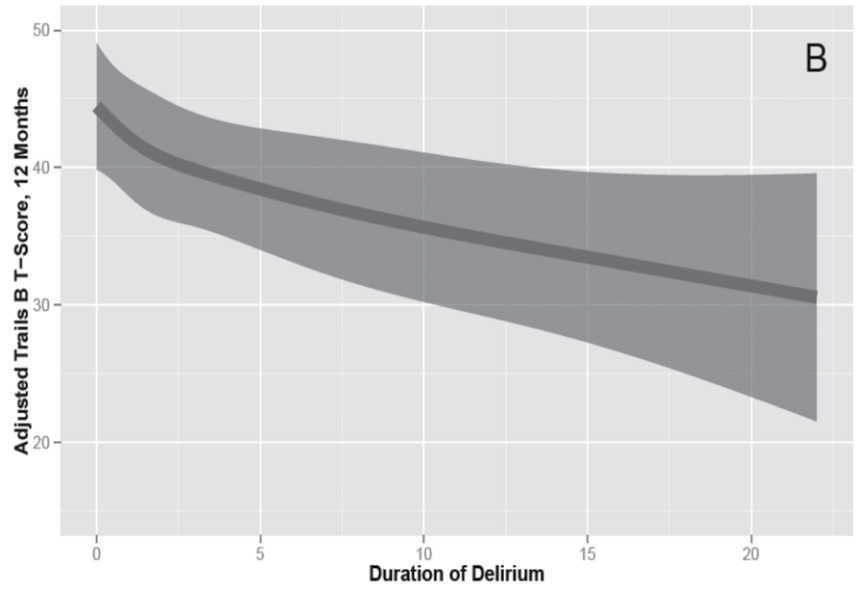


Figure 4. *(b) Delirium and executive function*



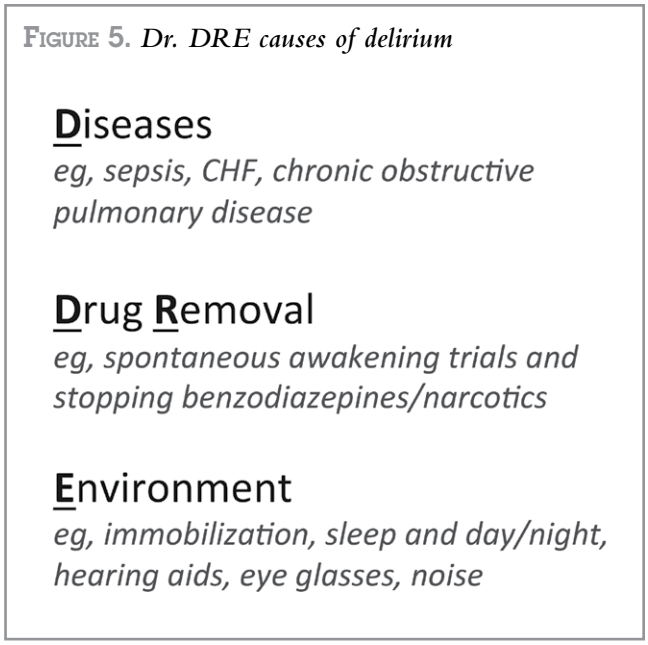
Abbreviations: RBANS (Repeatable Battery for the Assessment of Neuropsychological Status), MCI (Mild Cognitive Impairment), TBI (Moderate Traumatic Brain Injury), AD (Mild Alzheimer's Dementia), Trails B (Trail Making Test, Part B).
From Pandharipande PP, Girard TD, Jackson JC, et al. Long-term Cognitive Impairment After Critical Illness. *N Engl J Med*. 369, 1306-1316. Copyright © 2013 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

recommend the CAM-ICU[25,26] or the Intensive Care Delirium Screening Checklist (ICDSC).[27] The CAM-ICU can be completed in less than 1 minute and can be used in both verbal and nonverbal patients. The CAM-ICU measures 4 features of delirium: (1) acute change or fluctuation in mental status from baseline; (2) inattention, the cardinal and universal feature; (3) altered level of consciousness; and (4) disorganized thinking. A patient screens positive for delirium if features 1 and 2 are present along with either feature 3 or 4. The ICDSC is an 8-item checklist completed over an 8- to 24- hour period. One point is given for each checklist item present. The 8 items are level of consciousness, inattention, disorientation, hallucinations/delusions/psychosis, psychomotor agitation or retardation, inappropriate speech or mood, sleep-wake cycle disturbances, and symptom fluctuation. A score of 4 points or more constitutes a positive ICDSC and the presence of delirium.

Nonpharmacologic means of managing or treating delirium have been extensively studied in non-ICU settings,[28] and from such studies ICU teams have extrapolated information to develop programs for critically ill patients. These strategies focus on minimizing risk factors. For example, it may benefit the patient to reorient her or him repeatedly, provide cognitively stimulating activities multiple times a day, implement a nonpharmacologic sleep protocol, and apply early mobilization activities. Other strategies include removing catheters and physical restraints as early as safely possible, allowing patients to use eye glasses and magnifying lenses if needed, providing hearing aids and earwax disimpaction for patients warranting these, correcting dehydration quickly, using a scheduled pain management protocol, and minimizing unnecessary noise and stimuli. These strategies warrant further investigation in critically ill patients when bundled as a comprehensive nonpharmacologic protocol.

Regardless of what approach is taken with delirium, it can be very advantageous for the team to have a standardized, agreed-upon method of considering the differential diagnostic causes of a patient's delirium. For example, if delirium is present, the clinical team can briefly consider the most common risk factors using a simple mnemonic called the "Dr. DRE" (**Figure 5**).

Figure 5. *Dr. DRE causes of delirium*

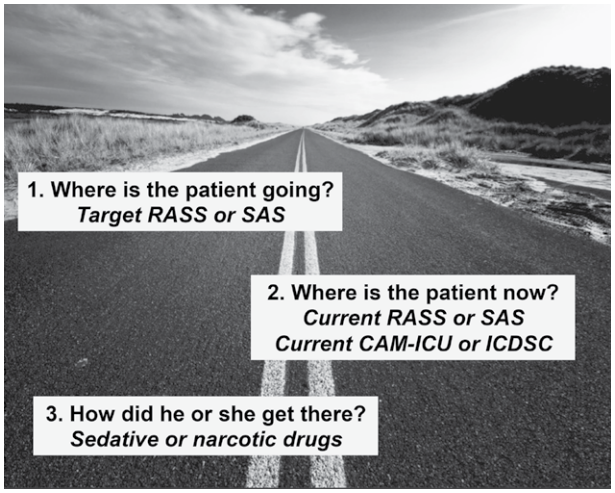


After reversible causes and modifiable risk factors have been addressed and nonpharmacologic strategies have been implemented, then and only then should pharmacologic interventions be considered. There are no published data determining a positive effect of haloperidol or atypical antipsychotics on decreasing the duration of delirium in adult ICU patients.[29-31] A small, prospective, randomized, double-blind, multicenter, placebo-controlled study randomized 18 patients to scheduled quetiapine and 18 patients to placebo.[32] Patients could receive intermittent haloperidol. The quetiapine group had a faster resolution of delirium compared with the placebo group (1 day vs 4.5 days, $P = 0.001$) and a shorter duration of delirium (36 days vs 120 days, $P = 0.006$). The quetiapine group required fewer days of as-needed haloperidol (3 vs 4 days). QT interval prolongation and extrapyramidal symptoms were similar between groups, but more somnolence was found with quetiapine (22% vs 11%, $P = 0.66$). This pilot is the only study to show shorter time to first treatment of delirium and decreased duration of delirium. The MIND-USA study, a multicenter, randomized, placebo-controlled, National Institutes of Health–sponsored investigation of delirious patients in medical and surgical ICUs with respiratory failure or shock, is currently examining the effect of haloperidol versus ziprasidone versus placebo on mortality, the number of days alive without delirium or coma, and long-term cognitive function.

The PAD guidelines recommend that patients with ongoing delirium who need more sedation should be considered for dexmedetomidine rather than benzodiazepines.[1] Three studies[33-35] have shown that patients were less likely to remain delirious with such an approach. The Maximizing Efficacy of Targeted Sedation and Reducing Neurological Dysfunction (MENDS) study found median days alive without delirium or coma to be 7 in the dexmedetomidine group compared with 3 in the lorazepam group ($P = 0.01$). Additionally, after the day of randomization, daily prevalence of delirium was lower in the dexmedetomidine versus lorazepam group ($P = 0.004$).[33] At baseline in the Safety and Efficacy of Dexmedetomidine Compared With Midazolam (SEDCOM) study, 60.3% of dexmedetomidine patients and 59.3% of midazolam patients were CAM-ICU positive. Prevalence of delirium during the study period was 54% of the dexmedetomidine group compared with 76.6% of the midazolam group ($P < 0.001$).[34] In the 2009 study by Ruokonen et al,[35] patients were more likely to be interactive if managed with the α_2-agonist dexmedetomidine. In the MIDEX study (which compared Midazolam vs. Dexmedetomidine, thus MIDEX), the composite outcome of agitation, anxiety, and delirium occurred in 27% of patients who received midazolam compared with 29% of patients who received dexmedetomidine ($P = 0.689$).[36] In PRODEX study (which compared Propofol vs. Dexmedetomidine, thus PRODEX), the outcomes of agitation, anxiety, and delirium (an agreed upon "composite outcome" treated as one outcome variable) occurred in 29% of patients who received propofol compared with 18% of patients who received dexmedetomidine ($P = 0.008$).[36] In summary, dexmedetomidine compared with benzodiazepines seems to lead to more favorable outcomes regarding delirium (eg, increased days alive without delirium and reduced daily prevalence of delirium), but this is not uniformly true of all investigations.

Perhaps the most important element of delirium management in the ICU setting involves communication among the team. To that end, many ICU teams now present on rounds using the "brain road map," which is a set of data containing 3 elements (**Figure 6**). At each bedside, the nurse (or another team member such as an intern or a pharmacist) will present the patient's (1) target RASS or SAS; (2) actual RASS or SAS, CAM-ICU, or ICDSC result; and (3) sedatives and narcotics received. This helps the team discuss the patient's cognitive status, compare it with the patient's desired cognitive status for that day, determine adjustments needed, and then explore the causes of delirium if the patient is CAM-ICU or ICDSC positive that day (using, for example, the Dr. DRE tool shown in **Figure 5**).

Figure 6. *Brain road map: a framework for bedside rounds*



Abbreviations: CAM-ICU, Confusion Assessment Method in the ICU; ICDSC, Intensive Care Delirium Screening Checklist; RASS, Richmond Agitation-Sedation Scale; SAS, Sedation Agitation Scale.

E: Early Mobility and Exercise

Early mobility is an important part of the ABCDEF bundle because it results in a decrease in ICU and hospital days of delirium. Studies have shown that early mobility is safe and realistic in critically ill patients.[2,37-39] Early mobility decreases days of delirium, days on mechanical ventilation, and ICU and hospital length of stay. Early mobility of patients can be conducted by any part of the interdisciplinary team, including nurses, physical therapists, occupational therapists, and physicians. Unresponsive patients with RASS –4 or /–5 can undergo passive range of motion or movement of all limbs in all cardinal directions

fully assisted. Patients with a RASS of –3 or –2 should undergo the passive range of motion activity as well attempt sitting if tolerated. Patients with a RASS of –1, 0, or +1 should be encouraged to stand, walk, and attempt activities of daily living.

F: Family Communication and Involvement

The last element of the ABCDEF bundle is family engagement, a component that cannot be overvalued. Family members play a large role in restoring health to the patient, and they should be engaged regularly with open and effective communication. Family members should be educated about the components and effectiveness of the bundle, as this will result in a line of open communication between the healthcare providers and the family. In addition, the family is well situated to hold the ICU team accountable to the many parts of the bundle since they spend so much time in the ICU with the patient and truly care (as a spokesperson for their often non-communicative loved one) what happens from a safety and comfort perspective.

It is possible that a delirious patient who does not respond to healthcare providers will respond to family members, due to the familiarity of their voices. The family should be encouraged to talk to such a patient: for example, reminding the patient of the day and date and talking about family and friends. Family members should speak softly and use simple words or phrases. They can also play the patient's favorite music and decorate the room with calendars, posters, or family pictures. It should be explained to family members that they might be asked to help calm the patient. Family members should be educated about delirium and its potential deleterious effects on the patient (posttraumatic stress disorder, depression, cognitive impairment) upon discharge from the hospital. Family members themselves may also suffer long-term psychological complications such as anxiety, depression, and posttraumatic stress disorder, commonly persisting for years. Frequent and effective communication and family presence on rounds have been recommended to maximize support to family members.

SUMMARY

For the sake of our patients' well-being, we must use the ABCDEF bundle to incorporate delirium awareness, monitoring, prevention, and treatment into ICU health systems. The 54-year-old male described at the beginning of this chapter had the ABCDEF bundle implemented through interdisciplinary efforts. After staff used CPOT assessments to ensure that pain was not contributing to his delirium, SATs were attempted and sedation was safely interrupted and not restarted; SBTs were attempted daily throughout the clinical course until the patient was extubated. Non-benzodiazepine sedation strategies were used, and mobility exercises were incorporated as tolerated even while the patient was receiving mechanical ventilation. This interdisciplinary approach was driven by the inquisitiveness of the patient and family (asking questions daily) as they helped the ICU team to do its best in serving the patient.

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