Liberating ICU Patients from Deep Sedation and Mechanical Ventilation—An Overview of Best Practices

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Objectives

- List the most valid and reliable ICU pain, sedation, and delirium assessment tools
- Define analgosedation or an analgesia first sedation strategy
- Define light vs. deep levels of sedation in ICU patients
- List 3 non-pharmacologic ICU delirium management strategies
- Name the elements of the ABCDEF bundle

Key words: pain, sedation, delirium, intensive care, guidelines

Pain, agitation, and delirium (PAD) occur frequently in critically ill patients. Severe pain is the most common memory that patients recall of their ICU stay. Pain often goes unrecognized and untreated, because many ICU patients can’t self-report their pain. Severe pain leads to both short- and long-term psychological and physical complications in ICU patients. Agitation and anxiety (due to pain, delirium, drug withdrawal, etc.) also occur often in critically ill patients, leading to hemodynamic instability, ventilator dyssynchrony, and device removal. Delirium occurs in the vast majority of ICU patients at some point during their ICU stay and is a risk factor for prolonged mechanical ventilation, increased ICU and hospital lengths of stay (LOS), increased healthcare costs, and increased hospital mortality in these patients. Delirious ICU patients also have a greater risk of developing long-term cognitive and physical dysfunction, a greater need for institutional care, and a shorter life expectancy following hospital discharge. Delirium can have a widely variable presentation, making it difficult to diagnose in these patients.

The Society of Critical Care Medicine (SCCM) recently published the ICU PAD clinical practice guidelines. These guidelines strongly advocate for optimizing pain management, avoiding deep sedation, and preventing and treating delirium in critically ill patients, to enable patients to actively participate in their care, promote their recovery, and reduce complications. The guidelines stress that clinicians should take an integrated and interdisciplinary approach to ICU pain, sedation, and delirium management and should link PAD management with ventilator weaning protocols and early mobility efforts, in order to achieve additional synergistic improvements in ICU patient outcomes. The PAD guideline recommendations have been incorporated into a single, integrated ICU PAD care bundle. The SCCM has also launched the ICU Liberation Campaign to promote widespread adoption of the ICU PAD care bundle, linking PAD management with spontaneous breathing trials and early mobility protocols through the use of the ABCDEF bundle checklist.

Successful implementation of the ICU PAD care bundle requires using a systematic approach, which begins with implementing the ICU PAD assessment tools, incorporating these PAD assessments into daily ICU patient care plans, developing and implementing unit-specific PAD treatment protocols, linking PAD management to...
ventilator weaning with daily spontaneous breathing trials and early mobility protocols, and engaging ICU patients and families. New evidence published since the guidelines further reinforces these principles. The use of effective implementation strategies will facilitate the translation of these recommendations into clinical practice.40,41 The purpose of this chapter is to provide an overview of these principles, including recent evidence published since the 2013 ICU PAD guidelines. Subsequent chapters provide greater detail on how to implement each bundle element.

**PAD ASSESSMENT TOOLS**

High doses of sedatives, opioids, and antipsychotics are typically administered to critically ill patients to prevent and treat agitation, often to the point of deep sedation, without first assessing patients. The

Abbreviations: SAT, spontaneous awakening trial; SBT, spontaneous breathing trial.

use of valid and reliable pain, sedation, and delirium assessment tools can help to facilitate pain management, prevent over sedation, and diagnose delirium in patients. Assessments should be performed across all 3 domains in order to optimize the care of each patient. Recommended PAD assessment tools can be found in the Appendices at the end of the book.

**Pain Assessment Tools**

Numerical rating scales (eg, Likert scales) are considered the gold standard for pain assessment. But numerical rating scales are difficult to use in ICU patients who are unable to self-report their pain, due to an altered level of consciousness, the use of sedatives or neuromuscular blocking agents, or mechanical ventilation. Changes in patients’ vital signs are often used as a surrogate indicator of pain. But blood pressure and heart rate correlate poorly with the presence or absence of pain in critically ill patients. In ICU patients who are unable to self-report pain, an observational or behavioral pain scale should be used instead. The ICU PAD guidelines include a strong recommendation for performing routine pain assessments in all ICU patients, using either a numerical rating scale (NRS) for ICU patients who can self-report their pain or a behavioral pain scale for those patients who cannot self-report.

Although most ICUs currently use an NRS for pain assessment, recent surveys reveal that most ICUs still do not use behavioral pain scales to assess pain in ICU patients who cannot self-report. Implementing behavioral pain scales improves both ICU pain management and patient outcomes, reduces the use of analgesic and sedative agents, and shortens the durations of mechanical ventilation and ICU length of stay. A 0–10 visually enlarged, laminated NRS is the most sensitive and specific tool for detecting significant pain in critically ill patients who can self-report. The Behavioral Pain Scale (BPS) and the Critical Care Pain Observation Tool (CPOT) are the most valid and reliable observational pain assessment tools for use in ICU patients who cannot self-report. Significant pain requiring treatment is indicated when a patient self-reports a pain score of 4 or higher (NRS range = 0–10) or when a patient who cannot self-report has either a BPS score of 6 or higher (BPS range = 3–12) or a CPOT score of 3 or higher (CPOT range = 0–8). Behavioral pain scales should not be used to validate a patient’s self-reported pain score. Pain assessments should be performed in patients at least 4 times per nursing shift, and more frequently if needed.

**Sedation Assessment Tools**

Until recently, there has been no clear consensus on the definition of “light” versus “deep” sedation in ICU patients. If ICU patients are to be reliably assessed for pain and delirium, or if they are to actively participate in ventilator weaning trials and early mobility efforts, patients must be awake and aware enough to follow commands. The PAD guidelines define light sedation as a level of sedation that allows the patient to perform any 3 of the following 5 actions upon request: open eyes, maintain eye contact, squeeze hand, stick out tongue, or wiggle toes. This definition of light sedation goes well beyond patients being merely “sleepy but arousable.”

The use of a valid and reliable sedation scale to assess depth of sedation can significantly reduce the incidence of deep sedation in ICU patients. Hager and colleagues showed that routinely monitoring depth of sedation in ICU patients with acute lung injury, targeting a light level of sedation where patients were “alert and calm,” significantly improved ICU sedation management and clinical outcomes in these patients. Sedation monitoring also significantly reduced the use of continuous IV infusions of opioids and benzodiazepines, more than doubled the number of patients who were lightly sedated, and increased the percentage of patients who were awake and not delirious from 0% to 19% ($P < 0.001$). Despite the benefits of using sedation scales, recent surveys suggest that up to 30% of adult ICUs still do not routinely use these scales to assess depth of sedation in their patients, and in the ICUs that do use sedation scales, most ICUs do not use the most valid and reliable sedation scales available. The PAD guidelines includes a strong recommendation for routinely assessing depth of sedation in all ICU patients.

A wide variety of sedation scales have been developed for use in the ICU. The most valid and reliable sedation assessment tools are the Richmond
The Agitation-Sedation Scale (RASS) and the Sedation-Agitation Scale (SAS). The RASS scale ranges from −5 (unarousable) to +4 (combative). The SAS scale ranges from 1 (unarousable) to 7 (dangerously agitated). The ICU PAD guidelines define light sedation as either RASS = −2 to 0 or SAS = 3 to 4. This level of sedation allows patients to purposely follow commands without agitation. With few clinical exceptions (e.g., increased intracranial pressure, refractory status epilepticus, severe acute respiratory failure, or pharmaceutically induced neuromuscular blockade), this level of light sedation should be the goal for the vast majority of ICU patients. Sedation assessments should be performed in patients at least 4 times per nursing shift and more frequently as needed.

**Delirium Assessment Tools**

Reliably diagnosing delirium in ICU patients is essential for the prompt treatment of delirium and to improve delirium-related outcomes. ICU nurses and physicians attempting to diagnose delirium based on clinical judgment alone overlook more than two-thirds of ICU patients who are actually delirious. The use of a valid and reliable delirium assessment tool can significantly improve the detection and diagnosis of delirium in ICU patients. The ICU PAD guidelines include a strong recommendation that all ICU patients be routinely assessed for delirium using a valid and reliable delirium assessment tool. Pun and Devlin recently outlined effective strategies for implementing delirium assessment tools in the ICU.

The Confusion Assessment Method in the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are considered to be the most valid and reliable delirium assessment tools for use in adult ICU patients. A patient is considered to be delirious if they are CAM-ICU positive or their ICDSC score is 4 or higher (ICDSC scale range = 0–8). It is impossible to perform delirium assessments in deeply sedated patients (i.e., RASS = −4 to −5 or SAS = 1 to 2), further making the case for maintaining a light level of sedation in most ICU patients. Delirium assessments should be routinely performed in all ICU patients, using either the CAM-ICU or the ICDSC tool, at least once a nursing shift, and more often as needed.

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**ICU PAD MANAGEMENT STRATEGIES**

It is not enough for ICU nurses to perform these bedside PAD assessments if providers do not use the information. PAD assessments should be routinely discussed on ICU rounds and should drive PAD treatment decisions tailored to each individual ICU patient, based on ICU-specific PAD treatment protocols. PAD protocols that facilitate the transfer of evidence-based best practices to the bedside can limit practice variation, enhance provider communication, reduce treatment delays, improve patient outcomes, and facilitate quality improvement efforts.

Mansouri and colleagues recently demonstrated significant improvements in patient outcomes when ICU patients were managed using a comprehensive ICU PAD treatment protocol that was based on routine pain (NRS and BPS), sedation (RASS), and delirium (CAM-ICU) assessments. Patients managed with a PAD protocol had a greater than 50% reduction in their duration of mechanical ventilation (P = 0.038), a 43% reduction in their ICU LOS (P < 0.001), and a 48% reduction in ICU mortality (P = 0.046).

Developing an integrated ICU PAD management protocol poses significant challenges, given the tremendous variability between ICU cultures, staffing models, provider practice patterns, and ICU patient populations. An effective strategy is to create an evidence-based, institutionally specific PAD protocol that integrates pain, sedation, and delirium management using an interdisciplinary team-based approach. PAD protocols that work well in one ICU may not work well elsewhere. Protocols should be adapted to individual hospital formularies, ICU cultures, and patient populations, avoiding a one-size-fits-all approach. Protocols also should be interdisciplinary in their development and application and should not be viewed simply as “nursing protocols.” Common elements of any PAD protocol should include emphasizing pain management over sedation, establishing light sedation as the norm in most patients, and emphasizing non-pharmacologic over pharmacologic delirium management strategies.
Optimizing Pain Management

Pain should be assessed and treated before ICU patients are sedated. A recent systematic review of the effects of analgesia-first sedation strategies (ie, analgosedation) on ICU patient outcomes concluded that making pain management a priority over sedation significantly reduces the duration of mechanical ventilation and ICU LOS.74 ICU patients, including those who are mechanically ventilated, may require little or no sedative medications once their pain is well controlled.51,75 Preemptive analgesia should be provided to patients prior to performing invasive or painful procedures. Preemptive relaxation therapy can augment analgesic medications administered before patients undergo painful procedures (eg, chest tube removal).76

All significant pain (ie, NRS ≥ 4, BPS ≥ 6, or CPOT ≥ 3) should be treated promptly (< 30 minutes) and reassessed within 30 minutes of treatment to determine analgesic efficacy. Parenteral opioids are the first-line agents for treating non-neuropathic pain, and enteral gabapentin and carbamazepine are the first-line treatments for neuropathic pain (opioids should only be considered as adjunctive agents for the treatment of neuropathic pain). Non-opioids (eg, IV acetaminophen, nonsteroidal anti-inflammatory drugs, ketamine) may be used as adjunctive agents to reduce opioid requirements and side effects. Regional analgesia techniques with proven efficacy are limited to the use of thoracic epidurals in patients with rib fractures or in patients following abdominal aortic aneurysm repair.

Optimizing Sedation Management

For several decades, the standard of ICU care has been to keep patients deeply sedated, using high doses of IV sedatives, opioids, and antipsychotics in order to prevent agitation, severe pain, ventilator dyssynchrony, physiological stress, and inadvertent device removal.77 But we now know that these benefits are far outweighed by the significant risks associated with deep sedation, including ventilator dependency, device-related infections, deep venous thrombosis, delirium, long-term physical and cognitive dysfunction, posttraumatic stress disorder, and death.78-86

Sedation protocols should therefore focus on limiting sedative exposure and avoiding deep sedation. Effective strategies include both targeted sedation strategies (TSS), where sedatives are titrated to consistently maintain a light level of sedation, and daily sedation interruptions (DSI), allowing patients to emerge from deep sedation once daily.87 Both TSS and DSI sedation management strategies can reduce sedative administration and shorten the duration of mechanical ventilation in critically ill patients. The ICU PAD guidelines recommended using either approach, because at the time of their publication there was no clear benefit to using TSS over DSI for sedation management.34 But more recent evidence suggests that deep sedation at any point during a patient’s ICU stay is an independent risk factor for worse clinical outcomes. Shehabi and colleagues80 found that early deep sedation (ie, RASS = −3 to −5 within 48 hours of starting sedation) was an independent predictor of delayed extubation (hazard ratio, 0.90; 95% CI, 0.87-0.94; P < 0.001) and an increased risk of in-hospital mortality (hazard ratio, 1.11; 95% CI, 1.02-1.20; P = 0.01) and 6-month mortality (hazard ratio, 1.08; 95% CI, 1.01-1.16; P = 0.026). Hager and colleagues57 implemented a sedation protocol targeting light sedation (ie, RASS = 0), using IV sedative boluses rather than IV infusions. Following implementation of this TSS protocol, patient wakefulness significantly increased (median RASS increased from −4 to −1.5, P < 0.001), while the incidence of delirium in awake ICU patients decreased (ie, from 19% to 0%, P < 0.001). Two recent meta-analyses comparing DSI to sedation management without DSI in critically ill adults also failed to demonstrate a clear benefit with DSI in terms of reducing the duration of mechanical ventilation, ICU or hospital length of stay, sedative administration, or mortality.88,89 A recent multicenter trial by Mehta and colleagues90 also found no clear benefit of combining TSS with DSI, in terms of the effects on duration of mechanical ventilation or ICU LOS, although this study suffered from significant methodological flaws.38 These recent findings suggest that ICU sedation protocols that continuously target a light level of sedation may be superior to daily sedative interruption alone and that combining these 2 practices offers no additional benefit, as long as light sedation levels are maintained.
Benzodiazepines, especially midazolam, are the most commonly used sedatives in ICU patients, followed by propofol and dexmedetomidine, while barbiturates, ketamine, and diazepam are used infrequently for ICU sedation.\textsuperscript{39,91-93} Despite the popularity of benzodiazepines, their use is associated with worse clinical outcomes in critically ill patients, compared with sedation with either propofol or dexmedetomidine. A recent meta-analysis showed that benzodiazepine sedation is associated with a longer duration of mechanical ventilation (1.9 days, \( P < 0.00001 \)) and ICU LOS (1.6 days, \( P = 0.001 \)) but no difference in delirium prevalence or mortality when compared with either propofol or dexmedetomidine sedation.\textsuperscript{94} Two large multicenter trials previously showed that delirium prevalence is \( \approx 20\% \) lower in ICU patients sedated with dexmedetomidine than in patients sedated with either lorazepam or midazolam.\textsuperscript{95,96} However, these data do not definitively prove that benzodiazepines cause delirium or that dexmedetomidine is either curative or protective against delirium. More recent evidence supports the notion that benzodiazepines do not cause delirium.\textsuperscript{97} Other evidence suggests that sedation with dexmedetomidine may shorten the duration of ICU delirium, compared with midazolam.\textsuperscript{98} A recent systematic review looking at the relationship between delirium and sedation with dexmedetomidine versus benzodiazepines, propofol, haloperidol, or morphine concluded that there is “no compelling evidence to support the use of dexmedetomidine for the prevention and treatment of ICU delirium” but that “dexmedetomidine has a promising role as a sedative agent, particularly in mechanically ventilated ICU patients with delirium or those at high risk for delirium.”\textsuperscript{99} This is consistent with the ICU PAD guideline recommendations for the use of dexmedetomidine for ICU sedation.\textsuperscript{34} A recent large multicenter trial comparing dexmedetomidine with propofol for ICU sedation showed no significant outcome differences (ie, duration of mechanical ventilation, ICU or hospital LOS, and mortality), although delirium prevalence was not measured in this study.\textsuperscript{100} A large multicenter trial (MENDS II) is currently underway comparing the effects of sedation with propofol versus dexmedetomidine on delirium prevalence, survival, and long-term cognitive function in septic ICU patients.\textsuperscript{101} Although duration of mechanical ventilation, ICU LOS, and delirium are important ICU clinical outcomes, they do not reflect the full complexity of issues surrounding sedative choice in individual patients. Given their anxiolytic, amnestic, and anticonvulsant properties, benzodiazepines remain an important class of drugs for sedating critically ill patients. They are the first-line agents for treating drug withdrawal syndromes and status epilepticus in critically ill patients.\textsuperscript{102-105} Benzodiazepines can also provide synergistic sedative effects in ICU patients who are unable to be effectively sedated with either dexmedetomidine and/or propofol.\textsuperscript{93,106}

### Optimizing Delirium Management

Critically ill patients typically have multiple baseline and acquired risk factors for developing ICU delirium.\textsuperscript{23,107} Targeting modifiable delirium risk factors, such as deep sedation, sleep deprivation, and immobility, can significantly reduce the risk of delirium in ICU patients.\textsuperscript{107} The ICU PAD guidelines recommend using non-pharmacologic strategies over pharmacologic strategies for both the prevention and the treatment of delirium. Effective non-pharmacologic delirium management strategies include patient reorientation, maintaining patients’ sleep-wake cycles, weaning patients expeditiously from mechanical ventilation, and early mobilization and exercise.\textsuperscript{35,108-113} Antipsychotics should be used only to treat severe or refractory delirium.

### Sleep Hygiene

Sleep deprivation and sleep fragmentation occur commonly in critically ill patients.\textsuperscript{114} The multifactorial causes of these abnormal sleep patterns include round-the-clock environmental stimuli, pain, sedatives and other medications, mechanical ventilation, and the underlying acute illness.\textsuperscript{115-117} Sleep deprivation leads to increased stress, anxiety, and immune suppression in these patients.\textsuperscript{116,118-120} Sleep deprivation is an independent risk factor for delirium, although the exact relationship between sleep deprivation and delirium is unknown.\textsuperscript{114,121,122} The ICU PAD guidelines include a strong recommendation for implementing non-pharmacologic ICU sleep hygiene programs that preserve patients’ sleep-wake cycles, based on somewhat weak evidence.\textsuperscript{34} More recent evidence
shows that implementing a multifaceted sleep program in the ICU (eg, establishing ICU “quiet time” at night; providing patients with earplugs, eye masks, and relaxation techniques at night; promoting daytime wakefulness in patients), decreases environmental stimuli at night, improves sleep quality and duration, and reduces the incidence and duration of delirium in ICU patients.109,111,123,124

The ICU PAD guidelines did not recommend the use of sleep-inducing medications in critically ill patients, due to a lack of evidence. But two medication treatment strategies are often used to facilitate “sleep” in critically ill patients: nighttime sedation125 and nighttime melatonin therapy. Data are lacking to support the practice of nighttime sedation, and sedative hypnotics actually disrupt electroencephalographic sleep patterns and interfere with restorative slow-wave and REM sleep.126-130 Dexmedetomidine may be less disruptive to normal sleep patterns than either benzodiazepines or propofol, which may also account for the lower delirium prevalence observed with dexmedetomidine versus benzodiazepine sedation.125 More studies are needed using gold-standard polysomnography monitoring techniques to delineate the true effects of nighttime sedation with dexmedetomidine on sleep and delirium.114,116

Melatonin is an endogenous neurohormone secreted by the pineal gland in response to changes in environmental patterns of light and dark. In healthy individuals, melatonin secretion peaks at night and helps to facilitate sleep. Critically ill patients have low nocturnal plasma melatonin concentrations and altered melatonin secretion patterns, due to their underlying severity of illness and medication effects.131-135 The extended-release form of oral melatonin mimics the endogenous pattern of melatonin production and is effective in treating disordered sleep patterns in healthy adults.136 The effects of melatonin on sleep quality in critically ill adults are unclear. Existing studies show mixed effects, with significant heterogeneity in study design and a lack of polysomnography data.137-139 A large, prospective trial is currently underway to assess the safety and efficacy of oral melatonin therapy for the treatment of sleep deprivation in critically ill adults, correlating polysomnography and sleep questionnaire data with the incidence and duration of delirium, duration of mechanical ventilation, ICU LOS, and mortality.140

Antipsychotics for ICU Delirium Management

Antipsychotics, and haloperidol in particular, are commonly used to treat delirium in critically ill patients.59,141,142 At the time the PAD guidelines were developed, there were no high-quality studies demonstrating the safety and efficacy of haloperidol, and only a few small studies had examined the safety and efficacy of atypical antipsychotics for the treatment of ICU delirium.143 One large multicenter trial showed an increased mortality associated with rivastigmine for the treatment for ICU delirium.144 Given the lack of high-quality evidence, the ICU PAD guidelines did not include a specific recommendation for the use of antipsychotics for the treatment of ICU delirium. Several recent systematic reviews and meta-analyses have reached similar conclusions.145-147 A large, multicenter, prospective randomized controlled trial is currently underway to determine the safety and efficacy of haloperidol versus ziprasidone versus placebo for the treatment of delirium in critically ill adults and to examine the impact of these delirium treatment regimens on ICU LOS, survival, and long-term cognitive function in patients.148 If antipsychotics are used to treat delirium, patients should be monitored for prolonged QT syndrome, which can lead to lethal ventricular arrhythmias in critically ill patients.149-153 There is no evidence that patients who develop delirium during their ICU stay require long-term treatment with antipsychotics once the delirium resolves. Antipsychotics should be discontinued 48 hours after a patient is no longer delirious.154 Jasiak and colleagues155 found that 50% of patients were transferred from the ICU while still receiving antipsychotics prescribed in the ICU for delirium, and 33% of these patients were discharged to home still receiving antipsychotics.

The ICU PAD guidelines offered no recommendations for using antipsychotic medications for delirium prophylaxis, due to a lack of evidence. But more recent evidence suggests that antipsychotics may be effective in preventing ICU delirium. Two recent studies found that prophylactic haloperidol may reduce the incidence and duration of delirium in ICU patients at
high risk for delirium.156,157 But a third study showed no clear effect on delirium prevention with either haloperidol or ziprasidone treatment compared with a placebo.158 A large multicenter, randomized controlled trial is now underway to assess the safety and efficacy of prophylactic haloperidol for the prevention of delirium in a more heterogeneous population of ICU patients.159 Only limited data exist on the use of atypical antipsychotics for ICU delirium prophylaxis. A recent systematic review and meta-analysis of 13 delirium prophylaxis studies (involving dexamethasone, rivastigmine, risperidone, ketamine, dexmedetomidine, propofol, and clonidine) demonstrated a pooled delirium risk reduction of 43%.157 Only 2 of these studies examined the efficacy of atypical antipsychotics, specifically risperidone, for delirium prophylaxis.160,161 Pooled data from these 2 studies (N = 227) showed that risperidone reduced the risk of delirium by almost two-thirds in these patients.147 More studies are needed to determine whether these results are generalizable to a more diverse ICU patient population.

Multimodal ICU Delirium Management Strategies

Once an ICU patient is diagnosed with delirium, the first step is to rule out or eliminate all contributing factors (ie, sepsis, shock, hypoglycemia or hyperglycemia, electrolyte abnormalities, hypoxia, hypercarbia, pain, drug withdrawal, decompensated psychiatric illness). Discontinue any deliriogenic medications, if possible (eg, ipratropium, H2 blockers, metoclopramide, corticosteroids). Consider switching from benzodiazepines to dexmedetomidine for sedation. Treat persistent delirium using non-pharmacologic treatment strategies first, such as the following: (1) frequently reorient ICU patients using a multimodal reorientation strategy108 and give them access to their eyeglasses and hearing aids, if needed; (2) maintain patients’ sleep-wake cycles by minimizing environmental and procedural disturbances at night using a multimodal sleep hygiene program, and provide patients with eye masks and earplugs at night109-111; (3) facilitate weaning from mechanical ventilation with daily spontaneous breathing trials (SBTs)111; and (4) advance patients’ mobility during the day as tolerated, with the ultimate goal of getting patients out of bed each day, even if they are intubated and mechanically ventilated.35,112,162 Use antipsychotics sparingly, monitor these patients for prolonged QT intervals, and discontinue antipsychotics once the patient’s delirium symptoms have resolved.

A multimodal approach to delirium management can significantly reduce the incidence and duration of delirium in critically ill patients.107 A recent systematic review of 14 studies of multimodal ICU delirium care bundles demonstrated significant reductions in the incidence and duration of ICU delirium, the duration of mechanical ventilation, the incidence of deep sedation, ICU and hospital LOS, and mortality.163 The delirium care bundles also led to significant improvements in the functional status of patients at the time of hospital discharge. Effective bundle implementation strategies included structured quality improvement approaches with ongoing audit and feedback, the use of multidisciplinary care teams, intensive staff education and training programs, electronic reporting systems, and local support teams. One study conducting a cost-effectiveness analysis indicated an average reduction of $1,000 in hospital costs for each ICU patient treated with a multifaceted delirium management protocol.164 Two large multicenter trials are currently underway to assess the effects of implementing a multimodal delirium treatment protocol on the severity and duration of delirium, ICU LOS, and mortality in critically ill patients.165,166

LINKING PAD MANAGEMENT TO VENTILATOR WEANING AND EARLY MOBILITY PROTOCOLS

Ventilator Weaning Protocols—Spontaneous Breathing Trials

The need for mechanical ventilation is the most common reason that patients are sedated in the ICU. Shortening the duration of mechanical ventilation will reduce patients’ exposure to sedatives and their associated complications. The use of respiratory therapist/nurse-driven weaning protocols that incorporate spontaneous breathing trials (SBTs) to assess patients’ work of breathing can hasten ventilator weaning and extubation and shorten ICU LOS.167-169 But it can be
difficult to perform SBTs in ICU patients who are deeply sedated and have significant respiratory depression. Linking sedation management to ensure that ICU patients are lightly sedated without agitation (ie, RASS = 0 to –2 or SAS = 3 to 4) during ventilator weaning trials can hasten weaning and extubation in these patients. Both DSIs (also called spontaneous awakening trials or SATs) and TSS sedation management strategies, when performed in conjunction with SBTs, accelerate the weaning process and further shorten the duration of mechanical ventilation in ICU patients.36,170-174 In the Awakening and Breathing Controlled (ABC) Trial, combining daily SATs with SBTs reduced the duration of mechanical ventilation by an additional 3 days ($P = 0.02$) and reduced both ICU LOS ($P = 0.01$) and hospital LOS by 4 days each ($P = 0.04$).36 Patients who received a combined daily SAT + SBT also had a 32% mortality risk reduction at 1 year compared with patients who received a daily SBT alone ($P = 0.01$). In the recent multicenter CDC Prevention Epicenters’ Wake Up and Breathe Collaborative, combining an SAT with an SBT resulted in a greater number of daily SBT trials being performed, reduced the risk of a ventilator-associated event by 38% ($P = 0.04$), and reduced infection-related ventilator-associated complications by 65% ($P = 0.01$).175 Duration of mechanical ventilation decreased by 2.4 days, ICU LOS by 3 days, and hospital LOS by 6.3 days when patients were managed with a combined SAT + SBT ($P < 0.0001$). Successful pairing of SAT with SBT protocols ultimately depends on protocol compliance, particularly with the SAT portion of the protocol. Provider reluctance to allow patients to emerge from deep sedation to enable them to participate in SBT trials may result in a failure to achieve similar improvements in ventilator weaning and the other ICU outcomes.176

Early Mobility

Critically ill patients frequently develop significant muscle weakness that can delay their recovery and worsen their clinical outcomes.177 The term ICU-acquired weakness has been used to describe this multifactorial syndrome, which results from the development of an acute myopathy and/or polyneuropathy in critically ill patients.178 Clinical risk factors include sepsis, inflammation, multiple-organ system failure, me-

chical ventilation (ie, due to diaphragmatic muscle atrophy and wasting), hyperglycemia, medications (ie, glucocorticoids, neuromuscular blocking agents >48 hours), female gender, and immobility (ie, enforced bed rest, restraints, and deep sedation).178 The incidence of ICU-acquired weakness ranges from 25% to 100% and negatively affects patients’ recovery.179,180 Patients with ICU-acquired weakness are $30\%$ less likely to successfully wean from mechanical ventilation ($P = 0.009$), $30\%$ less likely to survive their ICU stay ($P = 0.008$), and $31\%$ less likely to survive to hospital discharge ($P = 0.007$), with higher hospital costs and higher mortality rates at 1 year.181 Half of all ICU patients, regardless of age, are unable to return to their previous level of physical activity upon hospital discharge, due to persistent weakness and a lack of endurance.182-185

Efforts to mobilize patients early on during their ICU stay can help to prevent and treat ICU-acquired weakness, can significantly improve both short- and long-term clinical outcomes in these patients, and can reduce healthcare costs.36,37,83 A structured, multidisciplinary early mobility program nearly doubles the likelihood that both mechanically ventilated and non-ventilated ICU patients will receive active physical therapy and get out of bed much sooner during their ICU stay, without an increase in adverse events.37 Morris and colleagues showed that an ICU early mobility program reduced average ICU LOS by 1.4 days ($P = 0.025$) and hospital LOS by 3.3 days ($P = 0.006$) without significantly increasing costs, including ICU mobility team costs. Needham and colleagues found that early mobility of ICU patients reduced the incidence of deep sedation and sedative use while increasing patients’ functionality during their ICU stay without an increase in adverse events. In this study, delirium-free days in patients more than doubled ($P = 0.003$), ICU LOS decreased by 2.1 days ($P = 0.02$), and hospital LOS decreased by 3.1 days ($P = 0.03$). Winkelman and colleagues found that subjecting ICU patients to 20 minutes of daily exercise for 2 days or more decreased inflammatory dysregulation in ICU patients and reduced ICU LOS by 5 days ($P = 0.03$). Conversely, a lack of early mobility in ICU patients increases the risk of readmission or death during the first year post hospital discharge ($P < 0.05$).187
Despite these benefits, ICUs often struggle to make the necessary cultural and programmatic changes to implement a multidisciplinary ICU early mobility protocol. Traditional barriers to mobilizing critically ill patients include clinician concerns over patient safety (ie, cardiopulmonary instability, inadvertent extubation, dislodging tubes and catheters from patients) and the ICU staffing needed to get patients out of bed and ambulate them around the ICU. But several recent studies demonstrate that early mobility of ICU patients is safe, feasible, and economical in the ICU without significantly increasing staffing levels. Engel and colleagues recently described their experiences successfully implementing ICU early mobility programs at 3 different academic medical centers. These examples may provide useful templates for other ICUs struggling to overcome barriers to achieving early mobilization with their patients. Hodgson and colleagues recently published safety criteria for mobilizing ICU patients (based on expert consensus) and provided a reliable and feasible ICU mobility scale for measuring the highest level of mobility achieved by patients. Lord and colleagues have also developed a robust financial model that predicts significant net cost savings with only modest up-front hospital costs associated with an ICU early mobility program. Readers are referred to a later chapter that provides more details on successful strategies for implementing ICU early mobility programs.

**PUTTING IT ALL TOGETHER—THE ABCDEF BUNDLE**

Previous studies have demonstrated that linking ICU pain, sedation, and/or delirium management with ventilator weaning and/or early mobility results in additional synergistic improvements in ICU patient outcomes. Schweickert and colleagues combined a sedation protocol that included daily sedation interruptions with an ICU physical and occupational therapy program. They found that ICU duration was reduced by an average of 2 days ($P = 0.02$), ventilator-free days increased by 2.1 days ($P = 0.05$), and the odds of ICU survivors returning to an independent functional status at the time of hospital discharge nearly tripled ($P = 0.02$), compared with sedation management alone. Dale and colleagues implemented an integrated ICU PAD management protocol (ie, routine PAD assessments, an analgosedation/TSS sedation protocol targeting light sedation, and a multimodal delirium management protocol), linking it together with daily SATs and SBTs. Following protocol implementation, ICU patients were more likely to receive routine PAD assessments, benzodiazepine use decreased by more than one-third ($P < 0.01$), and patients’ risk of developing delirium decreased by 33% ($P = 0.01$). Duration of mechanical ventilation decreased by nearly 20% ($P = 0.01$), ICU LOS decreased by 12.4% ($P = 0.04$), and hospital LOS decreased by 14.0% ($P = 0.02$). Balas and colleagues implemented an ICU PAD management protocol, bundled together with daily SATs and SBTs and an early mobility protocol. Following bundle implementation, patients were more likely to receive daily SATs and SBTs and to get out of bed, the risk of ICU patients developing delirium decreased by nearly 50% ($P = 0.03$), delirium duration decreased by 1 day ($P = 0.003$), and the duration of mechanical ventilation decreased by 3 days ($P = 0.04$). These improvements in ICU patient outcomes were achieved despite little difference in medication exposure between the pre- and post-implementation groups and despite incomplete bundle adherence.

The SCCM’s ICU Liberation Campaign is designed to promote widespread adoption of the ICU PAD care bundle, coordinating ICU PAD management with ventilator weaning and early mobility in critically ill patients. The ABCDEF bundle checklist has been designed to facilitate implementation of these protocols (Figure 2). If widely adopted, this bundled approach to ICU pain, sedation, and delirium management, linked with ventilator weaning, early mobility, and family engagement in the ICU, is expected to significantly improve short- and long-term ICU patient outcomes and reduce healthcare costs. Subsequent chapters detail effective strategies for implementing the ABCDEF bundle checklist in your ICUs.
SUMMARY

The ICU PAD guidelines strongly advocate for an integrated approach to managing pain, sedation, and delirium in the ICU—one that is based on the use of valid and reliable PAD assessment tools and that emphasizes both nonpharmacologic and pharmacologic PAD management strategies. The guidelines emphasize the importance of optimizing pain management first, avoiding deep sedation, and preventing and treating delirium in critically ill patients, thus enabling patients to actively participate in ventilator weaning efforts and early mobility activities. More recent evidence reinforces these recommendations while closing several evidence gaps.

REFERENCES


