SPECIAL FEATURE

Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit: Executive summary

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Objective. To revise the "Clinical Practice Guidelines for the Sustained Use of Sedatives and Analgesics in the Critically Ill Adult" published in *Critical Care Medicine* in 2002.

Methods. The American College of Critical Care Medicine assembled a 20-person, multidisciplinary, multi-institutional task force with expertise in guideline development, pain, agitation and sedation, delirium management, and associated outcomes in adult critically ill patients. The task force, divided into four subcommittees, collaborated over six years in person, via teleconferences, and via electronic communication. Subcommittees were responsible for developing relevant clinical questions, using the Grading of Recommendations Assessment, Development and Evaluation method (www.gradeworkinggroup.org) to review, evaluate, and summarize the literature, and to develop clinical statements (descriptive) and recommendations (actionable). With the help of a professional librarian and Refworks database software, they developed a Web-based electronic database of over 19,000 references extracted from eight clinical search engines, related to pain and analgesia, agitation and sedation, delirium, and related clinical outcomes in adult ICU patients. The group also used psychometric analyses to evaluate and compare pain, agitation/sedation, and delirium assessment tools. All task force members were allowed to review the literature supporting each statement and recommendation and provided feedback to the subcommittees. Group consensus was achieved for all statements and recommendations using the nominal group technique and the modified Delphi method, with anonymous voting by all task force members using E-Survey (www.esurvey.com). All voting was completed in December 2010. Relevant studies published after this date and prior to publication of these guidelines were referenced in the text. The quality of evidence for each statement and recommendation was ranked as high (A), moderate (B), or low/very low (C). The strength of recommendations was ranked as strong (1) or weak (2) and either in favor of (+) or against (–) an intervention. A strong recommendation (either for or against) indicated that the intervention's desirable effects either clearly outweighed its undesirable effects (risks, burdens, and costs) or it did not. For all strong recommendations, the phrase "We recommend . . ." is used throughout. A weak recommendation, either for or against an intervention, indicated that the tradeoff between desirable and undesirable effects was less clear. For all weak recommendations, the phrase "We suggest . . ." is used throughout. In the absence of sufficient evidence, or when group consensus could not be achieved, no recommendation (0) was made. Consensus based on expert opinion was not used as a substitute for a lack of evidence. A consistent method for addressing potential conflicts of interest was followed if task force members were coauthors of related research. The development of this guideline was independent of any industry funding.

Conclusion. These guidelines provide a roadmap for developing integrated, evidence-based, and patient-centered protocols for preventing and treating pain, agitation, and delirium in critically ill patients.

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Statements and recommendations

1. Pain and analgesia
   a. Incidence of pain
      i. Adult medical, surgical, and trauma intensive care unit (ICU) patients routinely experience pain, both at rest and with routine ICU care (B).
      ii. Pain in adult cardiac surgery patients is common and poorly treated; women experience more pain than men after cardiac surgery (B).
      iii. Procedural pain is common in adult ICU patients (B).
   b. Pain assessment
      i. We recommend that pain be routinely monitored in all adult ICU patients (+1B).
      ii. The Behavioral Pain Scale (BPS) and the Critical-Care Pain Observation Tool (CPOT) are the most valid and reliable behavioral pain scales for monitoring pain in medical, postoperative, or trauma (except for brain injury) adult ICU patients who are unable to self-report and in whom motor function is intact and behaviors are observable. Using these scales in other ICU patient populations and translating them into foreign languages other than French or English require further validation testing (B).
      iii. We do not suggest that vital signs (or observational pain scales that include vital signs) be used alone for pain assessment in adult ICU patients (–2C).
      iv. We suggest that vital signs may be used as a cue to begin further assessment of pain in these patients, however (+2C).
   c. Treatment of pain
      i. We recommend that preemptive analgesia and/or nonpharmacologic interventions (e.g., relaxation) be administered to alleviate pain in adult ICU patients prior to chest tube removal (+1C).
      ii. We suggest that for other types of invasive and potentially painful procedures in adult ICU patients, preemptive analgesic therapy and/or nonpharmacologic interventions may also be administered to alleviate pain (+2C).
      iii. We recommend that intravenous (i.v.) opioids be considered as the first-line drug class of choice to treat non-neuropathic pain in critically ill patients (+1C).
      iv. All available i.v. opioids, when titrated to similar pain intensity endpoints, are equally effective (C).
      v. We suggest that nonopioid analgesics be considered to decrease the amount of opioids administered (or to eliminate the need for i.v. opioids altogether) and to decrease opioid-related side effects (+2C).
      vi. We recommend that either enterally administered gabapentin or carbamazepine, in addition to i.v. opioids, be considered for treatment of neuropathic pain (+1A).
      vii. We recommend that thoracic epidural anesthesia/analgesia be considered for postoperative analgesia in

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Supporting organizations include the American College of Critical Care Medicine (ACCM) in conjunction with the Society of Critical Care Medicine (SCCM) and the American Society of Health-System Pharmacists (ASHP).

To minimize the perception of bias in these guidelines, individual task force members with a significant conflict of interest on a particular topic were recused from grading the literature, writing evidence summaries, and developing specific statements and recommendations on that topic. Final decisions regarding strength of evidence and strength of recommendations for all questions were voted on anonymously by all task force members.

Mr. Dasta has consultancies with Hospira, Axel Rx, Cadence Pharmaceuticals, and Pacira Pharmaceuticals and has received

patients undergoing abdominal aortic aneurysm surgery (+1B).

viii. We provide no recommendation for using a lumbar epidural over parenteral opioids for postoperative analgesia in patients undergoing abdominal aortic aneurysm surgery, due to a lack of benefit of epidural over parenteral opioids in this patient population (0,A).

ix. We provide no recommendation for the use of thoracic epidural analgesia in patients undergoing either intrathoracic or nonvascular abdominal surgical procedures, due to insufficient and conflicting evidence for this mode of analgesic delivery in these patients (0,B).

x. We suggest that thoracic epidural analgesia be considered for patients with traumatic rib fractures (+2B).

xi. We provide no recommendation for neuraxial/regional analgesia over systemic analgesia in medical ICU patients, due to lack of evidence in this patient population (0, No Evidence).

2. Agitation and sedation
   a. Depth of sedation versus clinical outcomes
      i. Maintaining light levels of sedation in adult ICU patients is associated with improved clinical outcomes (e.g., shorter duration of mechanical ventilation and a shorter ICU length of stay [LOS]) (B).
      ii. Maintaining light levels of sedation increases the physiological stress response, but is not associated with an increased incidence of myocardial ischemia (B).
      iii. The association between depth of sedation and psychological stress in these patients remains unclear (C).
      iv. We recommend that sedative medications be titrated to maintain a light rather than a deep level of sedation in adult ICU patients, unless clinically contraindicated (+1B).
   b. Monitoring depth of sedation and brain function
      i. The Richmond Agitation-Sedation Scale (RASS) and the Sedation-Agitation Scale (SAS) are the most valid and reliable sedation assessment tools for measuring quality and depth of sedation in adult ICU patients (B).
      ii. We do not recommend that objective measures of brain function (e.g., auditory evoked potentials [AEPs], Bispectral Index [BIS], Narcotrend Index [NI], Patient State Index [PSI], or state entropy [SE]) be used as the primary methods to monitor depth of sedation in noncomatose, nonparalyzed critically ill adult patients, as these monitors are inadequate substitutes for subjective sedation scoring systems (–1B).
      iii. We suggest that objective measures of brain function (e.g., auditory evoked potentials [AEPs], Bispectral Index [BIS], Narcotrend Index [NI], Patient State

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Index [PSI], or state entropy [SE]) be used as an adjunct to subjective sedation assessments in adult ICU patients who are receiving neuromuscular blocking agents, as subjective sedation assessments may be unobtainable in these patients (+2B).

iv. We recommend that EEG monitoring be used to monitor nonconvulsive seizure activity in adult ICU patients with either known or suspected seizures, or to titrate electrosuppressive medication to achieve burst suppression in adult ICU patients with elevated intracranial pressure (+1A).

c. Choice of sedative

i. We suggest that sedation strategies using nonbenzodiazepine sedatives (either propofol or dexmedetomidine) may be preferred over sedation with benzodiazepines (either midazolam or lorazepam) to improve clinical outcomes in mechanically ventilated adult ICU patients (+2B).

3. Delirium

a. Outcomes associated with delirium

i. Delirium is associated with increased mortality in adult ICU patients (A).

ii. Delirium is associated with prolonged ICU and hospital LOS in adult ICU patients (A).

iii. Delirium is associated with the development of post-ICU cognitive impairment in adult ICU patients (B).

b. Detecting and monitoring delirium

i. We recommend routine monitoring of delirium in adult ICU patients (+1B).

ii. The Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are the most valid and reliable delirium monitoring tools in adult ICU patients (A).

iii. Routine monitoring of delirium in adult ICU patients is feasible in clinical practice (B).

c. Delirium risk factors

i. Four baseline risk factors are positively and significantly associated with the development of delirium in the ICU: preexisting dementia, history of hypertension, alcoholism, and a high severity of illness at admission (B).

ii. Coma is an independent risk factor for the development of delirium in ICU patients (B).

iii. Conflicting data surround the relationship between opioid use and the development of delirium in adult ICU patients (B).

iv. Benzodiazepine use may be a risk factor for the development of delirium in adult ICU patients (B).

v. There are insufficient data to determine the relationship between propofol use and the development of delirium in adult ICU patients (C).

vi. In mechanically ventilated adult ICU patients at risk of developing delirium, dexmedetomidine infusions administered for sedation may be associated with a lower prevalence of delirium compared to benzodiazepine infusions (B).

d. Delirium prevention

i. We recommend performing early mobilization of adult ICU patients whenever feasible to reduce the incidence and duration of delirium (+1B).

ii. We provide no recommendation for using a pharmacologic delirium prevention protocol in adult ICU patients, as no compelling data demonstrate that this reduces the incidence or duration of delirium in these patients (0,C).

iii. We provide no recommendation for using a combined nonpharmacologic and pharmacologic delirium prevention protocol in adult ICU patients, as this has not been shown to reduce the incidence of delirium in these patients (0,C).

iv. We do not suggest that either haloperidol or atypical antipsychotics be administered to prevent delirium in adult ICU patients (–2C).

v. We provide no recommendation for the use of dexmedetomidine to prevent delirium in adult ICU patients, as there is no compelling evidence regarding its effectiveness in these patients (0,C).

e. Delirium treatment

i. There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients (No Evidence).

ii. Atypical antipsychotics may reduce the duration of delirium in adult ICU patients (C).

iii. We do not recommend administering rivastigmine to reduce the duration of delirium in ICU patients (–1B).

iv. We do not suggest using antipsychotics in pa-

tients at significant risk for torsades de pointes (i.e., patients with baseline prolongation of QTc interval, patients receiving concomitant medications known to prolong the QTc interval, or patients with a history of this arrhythmia) (–2C).

v. We suggest that in adult ICU patients with delirium unrelated to alcohol or benzodiazepine withdrawal, continuous i.v. infusions of dexmedetomidine rather than benzodiazepine infusions be administered for sedation to reduce the duration of delirium in these patients (+2B).

4. Strategies for managing pain, agitation, and delirium to improve ICU outcomes
   a. We recommend either daily sedation interruption or a light target level of sedation be routinely used in mechanically ventilated adult ICU patients (+1B).
   b. We suggest that analgesia-first sedation be used in mechanically ventilated adult ICU patients (+2B).
   c. We recommend promoting sleep in adult ICU patients by optimizing patients' environments, using strategies to control light and noise, clustering patient care activities, and decreasing stimuli at night to protect patients' sleep cycles (+1C).
   d. We provide no recommendation for using specific modes of mechanical ventilation to promote sleep in mechanically ventilated adult ICU patients, as insufficient evidence exists for the efficacy of these interventions (0, No Evidence).
   e. We recommend using an interdisciplinary ICU team approach that includes provider education, preprinted and/or computerized protocols and order forms, and quality ICU rounds checklists to facilitate the use of pain, agitation, and delirium management guidelines or protocols in adult ICUs (+1B).

Since these guidelines were last published, we have made significant advances in our understanding of how to provide physical and psychological comfort for patients admitted to the intensive care unit (ICU).[1] The development of valid and reliable bedside assessment tools to measure pain, sedation, agitation, and delirium in ICU patients has allowed clinicians to manage patients better and to evaluate outcomes associated with both nonpharmacologic and pharmacologic interventions.[2,3] Our expanded knowledge of the clinical pharmacology of medications commonly administered to treat pain, agitation, and delirium (PAD) in ICU patients has increased our appreciation for both the short- and long-term consequences of prolonged exposure to these agents.[4-6] We have learned that the methods of administering and titrating these medications can affect patient outcomes as much as drug choice.[7-16] For most ICU patients, a safe and effective strategy that ensures patient comfort while maintaining a light level of sedation is associated with improved clinical outcomes.[9-13,16-20]

Ensuring that critically ill patients are free from pain, agitation, anxiety, and delirium at times may conflict with other clinical management goals, such as maintaining cardiopulmonary stability while preserving adequate end-organ perfusion and function.[21,22] Management goals may be further complicated by the growing number of "evidence-based" bundles and clinical algorithms, some of which have been widely adopted by regulatory agencies and payers.[23-30] Finally, tremendous worldwide variability in cultural, philosophical, and practice norms and in the availability of manpower and resources makes widespread implementation of evidence-based practices challenging.[31-36]

The goal of these clinical practice guidelines is to recommend best practices for managing PAD to improve clinical outcomes in adult ICU patients. We performed a rigorous, objective, transparent, and unbiased assessment of the relevant published evidence. We balanced this evidence against the values and preferences of ICU patients, family members, caregivers, and payer and regulatory groups and important ICU clinical outcomes to develop relevant statements and recommendations that can be applied at the bedside.

The scope of these guidelines includes short- and long-term management of PAD in both intubated and nonintubated adult medical, surgical, and trauma ICU patients. These guidelines only briefly address the topic of analgesia and sedation for procedures, which is described in more detail in the American Society of Anesthesiologists guidelines on conscious sedation.[37] The American College of Critical Care Medicine is currently developing separate guidelines on analgesia and sedation for pediatric ICU patients.

This version of the guidelines places a greater emphasis on the psychometric aspects of PAD monitoring tools. It includes both pharmacologic and nonpharmacologic approaches to manage PAD in ICU patients. There is also greater emphasis placed on preventing, diagnosing, and treating delirium, reflecting our growing understanding of this disease process in critically ill patients. These guidelines are meant to help clinicians take a more integrated approach to manage PAD in critically ill patients. Clinicians should adapt these guidelines to the context of individual patient care needs and the available resources of their lo-

cal health care system. They are not meant to be proscriptive or applied in absolute terms.

References

1. Jacobi J, Fraser GL, Coursin DB et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med.* 2002; 30:119-41.
2. Chanques G, Jaber S, Barbotte E et al. Impact of systematic evaluation of pain and agitation in an intensive care unit. *Crit Care Med.* 2006; 34:1691-9.
3. Payen JF, Bosson JL, Chanques G et al. Pain assessment is associated with decreased duration of mechanical ventilation in the intensive care unit: a post hoc analysis of the DOLOREA study. *Anesthesiology.* 2009; 111:1308-16.
4. Vasilevskis EE, Ely EW, Speroff T et al. Reducing iatrogenic risks: ICU-acquired delirium and weakness—crossing the quality chasm. *Chest.* 2010; 138:1224-33.
5. Riker RR, Fraser GL. Altering intensive care sedation paradigms to improve patient outcomes. *Crit Care Clin.* 2009; 25:527-38, viii-ix.
6. Arnold HM, Hollands JM, Skrupky LP et al. Optimizing sustained use of sedation in mechanically ventilated patients: focus on safety. *Curr Drug Saf.* 2010; 5:6-12.
7. Arabi Y, Haddad S, Hawes R et al. Changing sedation practices in the intensive care unit—protocol implementation, multifaceted multidisciplinary approach and teamwork. *Middle East J Anesthesiol.* 2007; 19:429-47.
8. Arias-Rivera S, Sánchez-Sánchez Mdel M, Santos-Díaz R et al. Effect of a nursing-implemented sedation protocol on weaning outcome. *Crit Care Med.* 2008; 36:2054-60.
9. Brattebø G, Hofoss D, Flaatten H et al. Effect of a scoring system and protocol for sedation on duration of patients' need for ventilator support in a surgical intensive care unit. *BMJ.* 2002; 324:1386-9.
10. Brook AD, Ahrens TS, Schaiff R et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation. *Crit Care Med.* 1999; 27:2609-15.
11. De Jonghe B, Bastuji-Garin S, Fangio P et al. Sedation algorithm in critically ill patients without acute brain injury. *Crit Care Med.* 2005; 33:120-7.
12. Quenot JP, Ladoire S, Devoucoux F et al. Effect of a nurse-implemented sedation protocol on the incidence of ventilator-associated pneumonia. *Crit Care Med.* 2007; 35:2031-6.
13. Robinson BR, Mueller EW, Henson K et al. An analgesia-delirium-sedation protocol for critically ill trauma patients reduces ventilator days and hospital length of stay. *J Trauma.* 2008; 65:517-26.
14. 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 Breathing Controlled trial): a randomised controlled trial. *Lancet.* 2008; 371:126-34.
15. Kress JP, Pohlman AS, O'Connor MF et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med.* 2000; 342:1471-7.
16. Mehta S, Burry L, Martinez-Motta JC et al. A randomized trial of daily awakening in critically ill patients managed with a sedation protocol: a pilot trial. *Crit Care Med.* 2008; 36:2092-9.
17. Adam C, Rosser D, Manji M. Impact of introducing a sedation management guideline in intensive care. *Anaesthesia.* 2006; 61:260-3.
18. Bucknall TK, Manias E, Presneill JJ. A randomized trial of protocol-directed sedation management for mechanical ventilation in an Australian intensive care unit. *Crit Care Med.* 2008; 36:1444-50.
19. Elliott R, McKinley S, Aitken LM et al. The effect of an algorithm-based sedation guideline on the duration of mechanical ventilation in an Australian intensive care unit. *Intensive Care Med.* 2006; 32:1506-14.
20. Treggiari MM, Romand JA, Yanez ND et al. Randomized trial of light versus deep sedation on mental health after critical illness. *Crit Care Med.* 2009; 37:2527-34.
21. Griffiths RD, Jones C. Seven lessons from 20 years of follow-up of intensive care unit survivors. *Curr Opin Crit Care.* 2007; 13:508-13.
22. Milbrandt EB, Angus DC. Bench-to-bedside review: critical illness-associated cognitive dysfunction—mechanisms, markers, and emerging therapeutics. *Crit Care.* 2006; 10:238.
23. Larson MJ, Weaver LK, Hopkins RO. Cognitive sequelae in acute respiratory distress syndrome patients with and without recall of the intensive care unit. *J Int Neuropsychol Soc.* 2007; 13:595-605.
24. Jones C, Griffiths RD, Humphris G et al. Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. *Crit Care Med.* 2001; 29:573-80.
25. Schelling G, Stoll C, Haller M et al. Health-related quality of life and post-traumatic stress disorder in survivors of the acute respiratory distress syndrome. *Crit Care Med.* 1998; 26:651-9.
26. Swaiss IG, Badran I. Discomfort, awareness and recall in the intensive care—still a problem? *Middle East J Anesthesiol.* 2004; 17:951-8.
27. Hopkins RO, Weaver LK, Collingridge D et al. Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 2005; 171:340-7.
28. Jones C, Griffiths RD, Slater T et al. Significant cognitive dysfunction in non-delirious patients identified during and persisting following critical illness. *Intensive Care Med.* 2006; 32:923-6.
29. Jones C, Bäckman C, Capuzzo M et al. Precipitants of post-traumatic stress disorder following intensive care: a hypothesis generating study of diversity in care. *Intensive Care Med.* 2007; 33:978-85.
30. Davydow DS, Gifford JM, Desai SV et al. Posttraumatic stress disorder in general intensive care unit survivors: a systematic review. *Gen Hosp Psychiatry.* 2008; 30:421-34.
31. Rello J, Lode H, Cornaglia G et al. A European care bundle for prevention of ventilator-associated pneumonia. *Intensive Care Med.* 2010; 36:773-80.
32. Tufano R, Piazza O, De Robertis E. Guidelines and the medical "art." *Intensive Care Med.* 2010; 36:1612-3.
33. Bellomo R, Stow PJ, Hart GK. Why is there such a difference in outcome between Australian intensive care units and others? *Curr Opin Anaesthesiol.* 2007; 20:100-5.
34. Rello J, Lorente C, Bodí M et al. Why do physicians not follow evidence-based guidelines for preventing ventilator-associated pneumonia? A survey based on the opinions of an international panel of intensivists. *Chest.* 2002; 122:656-61.
35. Hicks P, Cooper DJ, for the Australian and New Zealand Intensive Care Society (ANZICS) Board and Clinical Trials Group Executive Committee: the Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Resusc.* 2008; 10:8.
36. Orford NR, Faulkner C, Flintoff W et al. Implementation and outcomes of a severe sepsis protocol in an Australian tertiary hospital. *Crit Care Resusc.* 2008; 10:217-24.
37. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology.* 2002; 96:1004-17.