Ten Myths and Misconceptions Regarding Pain Management in the ICU

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Objectives: The aim of this article is to expose common myths and misconceptions regarding pain assessment and management in critically ill patients that interfere with effective care. We comprehensively review the literature refuting these myths and misconceptions and describe evidence-based strategies for improving pain management in the ICU.

Data Sources: Current peer-reviewed academic journals, as well as standards and guidelines from professional societies.

Study Selection: The most current evidence was selected for review based on the highest degree of supportive evidence.

Data Extraction: Data were obtained via medical search databases, including OvidSP, and the National Library of Medicine's MEDLINE database via PubMed.

Data Synthesis: After a comprehensive literature review, conclusions were drawn based on the strength of evidence and the most current understanding of pain management practices in ICU.

Conclusions: Myths and misconceptions regarding management of pain in the ICU are prevalent. Review of current evidence refutes these myths and misconceptions and provides insights and recommendations to ensure best practices. (*Crit Care Med* 2015; 43:2468–2478) **Key Words:** analgesia; analgesics; critical care; pain assessment; pain management; quality improvement

espite expanding knowledge of the physiologic effects of pain, availability of dependable tools for pain assessment, and evidence-based guidelines for

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analgesic management, pain is common and often undertreated in critically ill patients. In any setting, pain management can be complex and challenging. Pain may be acute, chronic, or acute on chronic and arise from somatic, visceral, neuropathic, and/or psychogenic sources. In the critically ill patient, mechanical ventilation, hemodynamic instability, impaired communication, fatigue, depression, and altered mental status further complicate the accurate assessment of pain and efficacy of treatment. Frequent threats to mental and bodily integrity magnify the experience of pain, challenging clinicians to respond swiftly and thoughtfully. Successful analgesia demands a comprehensive appreciation for the etiologies of pain, vigilant clinical assessment, and personalized treatments. Multimodal approaches and expert consultation are sometimes needed to avoid long-term sequelae.

Commonly encountered myths and misconceptions, in combination with ingrained practices, may also interfere with effective pain management in the ICU. Recently, Peitz et al (1) reviewed myths regarding sedation and delirium in the critical care literature. Although the article included some discussion of pain in nonsurgical patients and the effects of analgesic drug accumulation, the article was not specifically focused on pain management in critical care, and we wished to comprehensively review the topic. Furthermore, pain management is different from sedation management and should be evaluated and managed as a distinct goal of care.

In this review, we discuss 10 common myths and misconceptions regarding the management of pain in the ICU. Through a review of the most current and relevant literature, identified using OvidSP and the National Library of Medicine's MEDLINE database via PubMed, we debunk these myths and misconceptions and provide evidence-based strategies for improved pain management of the critically ill patient.

MYTH 1: THE MAJORITY OF CRITICALLY ILL PATIENTS RECEIVE ADEQUATE PAIN CONTROL

Nearly 50% of patients interviewed after their ICU stay rate their pain intensity as moderate to severe, both at rest and during commonly performed procedures (2–4). The prevalence of pain in medical and surgical ICU patients is similar and has multiple etiologies (**Table 1**) (4). Although underlying

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TABLE 1. Sources of Pain in the ICU

Disease process
Acute illness
Trauma
Surgical incision
Chronic illness and pain
Invasive therapy
Presence of endotracheal, nasogastric, and chest tubes
Invasive monitoring catheters
Urinary catheter
Other penetrating drains and catheters
Immobility
Ongoing mechanical ventilation
Insertion and removal of catheters and tubes
Daily care
Tracheal suctioning
Turning in bed
Wound dressing changes
Exacerbating factors
Altered sensorium or delirium
Impaired communication
Sleep deprivation
Preexisting chronic pain

illness, extensive surgery, invasive procedures, incisions, penetrating tubes, and catheters are recognized sources of pain, pains associated with routine ICU care, such as tracheal suctioning, turning and mobilization, and dressing changes, are often underappreciated by caregivers (5). Furthermore, immobility generates discomfort from musculoskeletal stiffness and wasting, neuropathies, and pressure ulcers. Pain associated with medical comorbidities and chronic pain states can be exacerbated by discontinuing regular analgesic medications as a result of incomplete drug history or concern for adverse medication side effects. Ongoing mechanical ventilation, sleep deprivation, and delirium further contribute to emotional and physical discomfort and heighten the perception of pain (6).

There are multiple obstacles to the provision of effective pain management in the ICU (**Table 2**) (7). Common providerrelated obstacles result from 1) failure to assess and acknowledge the existence of pain, 2) inadequate knowledge of the types and appropriate dosages of analgesics, 3) assignment of a low priority to pain management, and 4) fear of precipitating opioid addiction. These factors likely contribute to undesirable variation in pain management practice; there is considerable evidence that medical patients receive less analgesia than do surgical patients

TABLE 2. Barriers to Effective Pain Management in the ICU

Provider

Knowledge deficits regarding the pathophysiologic effects	
of pain and pain management principles	

Assignment of a low priority to pain management

Failure to assess and acknowledge the existence of pain

Failure to evaluate the effect of treatment

Failure to adjust management in a timely fashion

Inappropriate attitudes regarding the use of opioids

- Lack of knowledge of the types and appropriate dosages of analgesics
- Overconcern about the development of tolerance to analgesic medications

Subconscious reactions to "drug-seeking" behavior

Personal and cultural biases

Communication difficulties between the patient and the healthcare team

Healthcare system

- Inadequate quality improvement process for pain management
- Lack of accountability for unsatisfactory outcomes related to poorly managed pain
- Logistical hurdles to timely analgesic administration (e.g., increased nursing burdens)
- Underemphasized use of multidisciplinary approaches for pain management

Patient

Inability to report pain

Feelings that pain should be tolerated or is an inevitable part of the disease process

Fear of the consequences of reporting pain

Fear of side effects related to analgesic drugs

when undergoing identical procedures (4). Furthermore, medical patients are generally less likely to receive analgesia, independent of pain scores. Personal and cultural biases and communication difficulties between the patient and the healthcare team are additional provider-related barriers to pain management (8). Among the most common heath system–related obstacles are logistical hurdles related to timely analgesic administration (e.g., increased nursing burdens), inadequate quality improvement monitoring, and a lack of accountability for poorly managed pain.

Patient-related factors may also contribute to ineffective pain management. The effects of sedation or neurologic compromise may prevent verbal, behavioral, or physical expression of pain. Furthermore, patients may think that pain should be tolerated, feel that requests for pain medications are burdensome, or experience communication fatigue (9). Contributing

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to these obstacles is a lack of high-level evidence to guide treatment decisions specific to the critically ill population, and extrapolation of data from non-acute care settings may be inaccurate. Medical and surgical stabilization, along with awareness of analgesic side effects, must be balanced against harmful effects of untreated pain (10).

MYTH 2: PAIN DOES NOT AFFECT SHORT-AND LONG-TERM OUTCOMES

Untreated pain negatively impacts physiologic and psychologic functions in both the short term and the long term (**Fig. 1**). Many of these effects result from exacerbation of the stress response (11, 12). Pain activates the autonomic nervous system, elevating circulating catecholamines and stress hormones that cause vasoconstriction, impair tissue perfusion, and reduce tissue oxygen partial pressure (12, 13). This results in tachypnea, increased myocardial oxygen demand, activation of the reninangiotensin-aldosterone axis, and increased cytokine production (14). Furthermore, pain initiates metabolic disturbances, including altered glycemic control, enhanced catabolic state, hypercoagulability, and immune system dysfunction (13, 15).

Persistent pain inhibits effective coughing and deep breathing, predisposing patients to respiratory complications, such as atelectasis, pneumonia, hypoxemia, and hypercarbia. Over time, reduced adherence to physiotherapy leads to reduced mobility and musculoskeletal deconditioning. Chronic, persistent, and often neuropathic pain states may develop as a result of poorly controlled pain in the short term (16).

In addition to physiologic effects, there are also significant psychologic consequences resulting from unrelieved pain. Anxiety, depression, impaired sleep, and increased prevalence of nightmares, as well as feelings of demoralization, helplessness, and loss of autonomy, occur in the short and long terms (7, 17). Both patients and family members report pain as the most stressful experience both during and after ICU admission (7). As a result, memory of pain during an intensive care admission is an independent predictor of the development of posttraumatic stress disorder (18). Psychologic symptoms, such as depression or sleep disturbance, may not only be the consequences of poor pain control but may also play a role in central pain processing and exacerbate pain (19).

Although poor pain control is clearly associated with worse outcomes, evidence demonstrates that adequate analgesia is associated with improved outcomes (20–25). For example, neuraxial blockade has been shown to reduce the rate of amino acid oxidation and postsurgical catabolism, so-called proteinsparing effects. This reduces energy expenditure and preserves lean body mass, providing a more metabolically favorable state for recovery (26). Treating pain also reduces cortisol levels, reducing hyperglycemia and improving postoperative lymphocytic immune function (27).

Studies performed in surgical, trauma, and medical ICUs illustrate that a protocol-based approach to assess and manage pain, agitation, and delirium is associated with improved short-term and long-term outcomes, such as reduced duration of mechanical ventilation, infection rate, length of stay, health-care costs, and 30-day mortality (20–25). These benefits have been largely attributed to a reduction in the administration of sedative-hypnotic medications that results from appropriate administration of analgesic medications when pain is adequately prioritized, assessed, recognized, and treated (20–25).

MYTH 3: ACCURATE PAIN ASSESSMENT CANNOT BE PERFORMED IN CRITICALLY ILL PATIENTS BECAUSE PAIN IS SUBJECTIVE

Pain assessment in the ICU is often suboptimal, with infre-

quent assessments, poor documentation, and inconsistency in the use of assessment tools.

Pain assessments are inac-

curate up to 40% of the time and often underestimate pain, especially when pain scores are high (28, 29). Pain is unique to each individual, lacks linearity

between injury and severity, and is variably expressed. To address these challenges, vali-

dated assessment tools exist

to objectively quantify and

qualify pain for critically ill

standard for pain assessment.

Questioning the onset, loca-

tion, duration, intensity, and

quality of pain allows the clinician to differentiate between

possible causes and to consider

Self-reporting is the gold

patients.

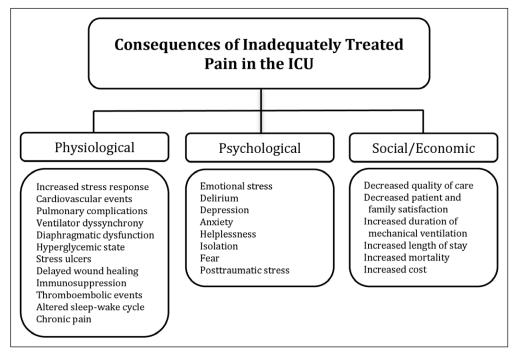


Figure 1. Consequences of inadequately treated pain in the ICU.

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appropriate interventions. Helping the patient identify exacerbating and relieving factors permits fine-tuning of analgesic care, and acknowledging the patient's experience of pain helps the clinician to solidify a therapeutic alliance.

Regardless of underlying cognitive status, clinicians should always attempt to elicit self-reporting of pain. For example, although the presence of delirium is associated with the failure to use a self-reported pain scale, the presence of delirium should not preclude clinicians from evaluating pain through patient self-reporting because pain can be associated with or precipitate delirium (30, 31). If pain is reported by a delirious patient, then the cause and reality of pain should be carefully investigated, as in any other instance of patient-reported pain.

Unidimensional tools evaluate a single aspect of pain, commonly intensity, and can be categorical (verbal rating and descriptor scales) or numerical. The Numerical Rating Scale (NRS) is a commonly used pain assessment tool that permits patients to rate pain on a numeric axis from zero (no pain) to 10 (worst pain imaginable). In a recent comparison of five selfreported pain intensity scales, the NRS was the most feasible (91%) and had the best negative predictive value (90%) (31). Although tools exist to evaluate multiple aspects of the pain experience (multidimensional), they are lengthy and often impractical to use in an intensive care setting.

Vital signs (blood pressure, heart rate, and respiratory rate) are widely used by clinicians for pain assessment (32). However, vital signs lack specificity for pain assessment since they can increase, decrease, or remain stable due to physiologic conditions unrelated to pain (33). Consequently, vital signs should not be used in isolation to assess pain; rather, they should be used as a cue for further investigations regarding the presence of pain (34).

In circumstances where self-reporting is not possible, pain assessment tools that incorporate behaviors and physiologic variables can be used. Of those developed and validated for ICU use, the Behavioral Pain Scale (BPS) and the Critical Care Pain Observation Tool (CPOT) have the strongest evidence for reliability and validity (23, 35-38). Both scales can be used in patients with artificial airways. The BPS evaluates three behavioral domains: facial expression, movement of upper limbs, and compliance with ventilation in response to movement and painful stimuli. Each behavioral domain is rated from one (no response) to four (full response), with a composite score ranging from three to 12. The CPOT evaluates four behavioral domains: facial expressions, movements, muscle tension, and ventilator compliance. Each component is rated from zero to two with a composite score ranging from zero to eight. If patients do not have an artificial airway, the BPS and CPOT include a vocalization domain to be assessed (35, 36).

Four additional BPSs, the Initial Nonverbal Pain Scale, the Revised Nonverbal Pain Scale, the Pain Behavioral Assessment Tool, and the Pain Assessment, Intervention, and Notation Algorithm, were also evaluated when establishing the 2013 Society of Critical Care Medicine (SCCM)/American College of Critical Care Medicine (ACCM) guidelines for management of pain, agitation, and delirium (39). In comparison, the CPOT and BPS demonstrated the most consistent evidence (highest validity and interrater reliability) in medical, surgical, and trauma ICU patient populations, and in particular, noncommunicative critically ill adults (39, 40). Other BPSs, such as the Nonverbal Pain Assessment Tool and the face, legs, activity, cry, consolability scale, similarly do not share the level of validation and reliability in the critically ill patient population compared with the CPOT and BPS (41–45).

Despite implementation of a robust and structured pain assessment tool, challenges may still arise in clinical practice. For example, a suffering patient may respond with a number that exceeds the upper scale limit (e.g., 12 out of 10). This signals the need to optimize analgesic therapy while exploring other psychologic underpinnings of pain (e.g., anxiety and fear) (46). Requesting further description of the pain experience can empower the patient to maintain an active role in pain management and ensures a more comprehensive understanding of pain-exacerbating phenomena (46). Assessment by family members or other individuals familiar with the patient, on the other hand, underestimates pain intensity nearly 50% of the time (47). Furthermore, behavioral expression of pain may be more challenging to interpret in special patient populations, such as critically ill burn patients (48).

MYTH 4: PAIN CONTROL IN THE ICU IS PRIMARILY THE NURSE'S RESPONSIBILITY

The bedside nurse plays an essential role in assessment and management of pain in critically ill patients. The importance of the role is emphasized by literature reporting that ICU physicians underevaluate patients' pain compared with nurses (5). However, the most effective approach to pain assessment and management in the ICU is a team approach (physician, nurse, and pharmacist) (49). In addition to a team approach, a structured and ongoing commitment to improving pain control within the ICU is needed. The American Pain Society (APS) has developed guidelines to improve the quality of pain management that may be applicable to the ICU setting (50). The APS guidelines first emphasize the reevaluation of current practices. A review of medication-prescribing habits and patterns, patient and family satisfaction data, and assessment of care team's knowledge, attitudes, and satisfaction detects areas to prioritize improvement efforts. From this information, structured approaches that incorporate evidence-based guidelines, algorithms, protocols, checklists, and daily pain goals can be established and implemented (50).

The SCCM/ACCM guidelines for management of pain, agitation, and delirium provide a practical and multifaceted strategy for ICU pain management by combining routine pain and sedation assessments with a structured, evidence-based pain management approach (39). Educating staff on pain assessment and management in intensive care is an essential component of a pain management quality improvement program and has been demonstrated to increase both the frequency of pain assessments and administration of analgesia to those experiencing pain (23). In addition, the availability of a formal acute pain service can improve outcomes and improve efficiency when patients are complex (7, 51).

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The application of quality improvement methodology also leads to effective system-based solutions (52, 53). With this approach, pain is viewed as a preventable adverse event, and quality improvement methods, such as the Plan-Do-Check-Adjust Cycle, are applied with proven treatments and recommended strategies to allow the integration of the best evidence into clinical practice (54). The use of pain assessment tools, for example, can be considered a quality-healthcare indicator, closely associated with the use of analgesics and sedatives, thereby resulting in better, measurable improvements in pain control and associated ICU outcomes.

MYTH 5: OPIOIDS ARE ALL THAT IS NEEDED FOR EFFECTIVE PAIN CONTROL IN THE ICU

Opioid receptors are found in the peripheral nervous system and CNS, and opioids that target those receptors have a long history of use in acute and chronic pain management. Despite their central role in pain management, opioids have a number of unwanted side effects that must be considered when designing an analgesic regimen. Opioids have the potential to depress respiratory drive, reduce gastric motility, and interfere with the provision of enteral nutrition (55). Some literature suggests that opioids are associated with immunosuppression (56). Although the risk of analgesia-associated immunosuppression could be detrimental in the critically ill population, it must be balanced against the risks of undertreated pain, which also has immunosuppressive effects.

Pain management may also be complicated by opioidinduced hyperalgesia (OIH), a phenomenon in which patients chronically receiving opioids become more sensitive to pain as a direct result of opioid therapy (57). With OIH, the use of opioids becomes a double-edged sword: opioid therapy provides analgesic effects initially but subsequently renders patients more sensitive to pain and aggravates their preexisting pain. Although the precise mechanism of OIH has not been elucidated, it is generally thought to result from neuroplastic changes in the peripheral nervous system and CNS that lead to sensitization of pronociceptive pathways (58).

The cornerstone of comprehensive, individualized pain management is multimodal analgesia (59). Multimodal analgesia focuses on the combination of different pharmacologic agents and techniques that produce analgesic effects at multiple levels along nociceptive pathways, via action on receptors within peripheral tissue, in the spinal cord, and at various levels within the brain. By following this concept, clinicians can provide potent, synergistic analgesia while minimizing the adverse effects of a given analgesic agent.

Multimodal therapy encompasses a wide range of medications, including opioids, nonsteroidal anti-inflammatory agents, acetaminophen, *N*-methyl-_D-aspartate (NMDA)-receptor antagonists, α_2 -adrenoceptor agonists, tricyclic antidepressants, antiepileptic medications, and painrelated techniques, such as neuraxial analgesia and peripheral nerve blocks. Multimodal therapy also includes optimal timing of these interventions. Although preemptive analgesia (the initiation of treatment before exposure to the painful stimulus) is not possible in trauma and many other forms of critical illness, preventive analgesia by reducing sustained pain within the ICU is often feasible. The data suggest that preventive analgesia provides benefit in acute and chronic pain by reducing both the peripheral sensitization from injury and the subsequent development of central sensitization (60).

Although the potential benefits of multimodal analgesia are clear, the literature indicates that nonopioid analgesics are less commonly used in critical care compared with other healthcare environments (61). The use of nonopioid analgesics is likely to be especially beneficial in cases where opioids are less effective, such as with the opioid-tolerant patient or the patient with neuropathic pain (62). Despite their benefits, many nonopioid analgesics have potential toxicities or drug interactions that may be exacerbated in critically ill patients who have impaired organ function and/or are receiving multiple medications. Consequently, when nonopioid analgesics are used as part of multimodal therapy, individual risk-benefit evaluations should be performed and regularly reassessed.

The contribution of central mechanisms to certain chronic pain phenotypes should also be appreciated (63). Nonopioid agents, such as antidepressants and gabapentanoids, aimed at centrally mediated pain pathways may improve both acute pain management during ICU stay and reduce chronic pain development after ICU stay. Although currently not approved by Food and Drug Administration in the United States, Nefopam, a centrally acting, nonopioid analgesic of the benzoxazocine class, improves pain in the critically ill and is widely used in Europe (64).

Regional analgesia (continuous epidural or peripheral nerve blocks) is commonly used to improve the efficacy of traditional analgesic interventions in postoperative patients, but its use in the ICU has been limited (65). Potential benefits of regional anesthesia in critically ill patients include reduced pulmonary complications, a less sedated and more lucid mental state, improved gastrointestinal and hepatic microcirculation, and anti-inflammatory and antithrombotic effects (65). Although regional anesthetic techniques might favorably affect outcomes, there is limited evidence supporting this assumption.

The 2013 SCCM/ACCM guidelines for management of pain, agitation, and delirium recommend the use of thoracic epidural anesthesia-analgesia in patients undergoing abdominal aortic surgery and for patients with rib fractures (39). Although there is minimal evidence to suggest that there is an increased risk of local and systemic infection solely attributable to indwelling pain catheters (65), comorbidities related to critical illness pose substantial risks for regional pain procedures. There may be technical challenges with patient positioning and block placement, increased risk for paresthesias or anatomical injury, increased chance of local anesthetic toxicity due to decreased metabolism, the presence of bacteremia and sepsis increasing the risk of procedural site infection, or coagulopathy increasing the risk of hematoma formation (66, 67).

Nonpharmacologic interventions may also be part of the multimodal approach to analgesia. Pain-modulating

interventions, such as application of heat or cold packs, massage, and acupuncture, reduce pain mediator release, thereby decreasing pain (68–70). Psychologic interventions, including the use of relaxation techniques and music therapy, may decrease pain intensity (71, 72). Despite limited evidence to support their benefits in the ICU, these interventions can be simple to implement, exhibit few side effects, and have been demonstrated to improve pain in other clinical settings.

MYTH 6: THERE IS A MAXIMUM DOSE OF OPIOIDS THAT SHOULD BE USED TO TREAT ACUTE PAIN

Despite receiving large doses of opioids, inadequate pain control may still occur in some patients such as those with opioid dependence, chronic pain requiring opioid therapy, substance abusers, or recovering substance abusers in opioid maintenance programs. In this setting, the source may be from increased nociceptive input, development of tolerance, or a pain-exacerbating psychologic process.

Evidence to guide analgesia in the critically ill opioid-dependent patient is limited and is therefore extrapolated from studies of individuals who receive opioid agonist therapies, such as methadone for the management of addiction. Studies have shown a lower tolerance for painful stimuli among opioiddependent patients receiving chronic methadone treatment when compared with controls (58,73). In addition, these opioiddependent patients achieve less robust and shorter responses to opioids and experience reduced analgesic effects despite serum morphine levels that are typically therapeutic for the nonopioiddependent patients (74). Patients maintained on opioid agonist therapy may develop cross-tolerance to other opioid agents, which must be accounted for when switching from one opioid to another (75). Patients with addiction and physical dependence to opioids are at risk for developing withdrawal symptoms if insufficient doses of opioids are administered.

The first step in successful management of acute pain in the opioid-dependent ICU patient is to determine baseline opioid use. For patients in opioid maintenance programs, the prescriber or program should be contacted to verify the maintenance regimen. Patients who are unable or unwilling to disclose opioid use must be monitored closely for inadequate pain control and for early signs of opioid withdrawal. Opioids are considered first-line therapy for the treatment of moderate-tosevere acute pain in patients with opioid dependence. Ideally, the preexisting opioid regimen or an equianalgesic dosage of an alternative opioid should be continued at admission to the ICU, with supplemental analgesia used as necessary.

Opioid agonists have no maximum dose or ceiling dose. The appropriate dose is the amount of opioid that controls pain with the fewest side effects. As a result of receptor down-regulation, opioid requirements often need to be increased 30% to 100% in comparison with requirements for opioid-naive patients (76). Patients receiving buprenorphine therapy for addiction create a distinct challenge for management of acute pain. Buprenorphine is a partial μ -opioid agonist with antagonist properties that can interfere with the analgesic

effectiveness of adjunct opioids. Substantially, increased doses of opioids may be needed in patients receiving buprenorphine to overcome the antagonist properties of the drug (77).

When opioid dose escalation fails to control pain, it is important to determine whether the lack of efficacy is related to tolerance or to OIH. If preexisting pain is undertreated or pharmacologic tolerance exists, then increasing the opioid dose will reduce pain. Conversely, OIH will worsen with increasing opioid dose. In opioid-tolerant patients, switching to an alternative opioid may improve analgesic efficacy (78). Incomplete cross-tolerance may enable a substitute opioid, "opioid rotation," to achieve improved pain relief at lower dosages, decreased toxicity, and better tolerability (79).

The lack of analgesic efficacy may occur despite aggressive escalation of opioid therapy, so multimodal pain management with nonopioid analgesics and nonpharmacologic strategies should be implemented. The addition of nonopioid medications (e.g., nonsteroidal anti-inflammatory agents, acetaminophen, anticonvulsants, antidepressants, and antipsychotics) to the maintenance opioid regimen can reduce the dose of supplemental opioids required (80). NMDA-receptor activation plays an important role in the development of tolerance; therefore, selecting an agent that blocks this receptor is ideal. Methadone is a µ-receptor agonist with NMDA-receptor antagonist activity that displays unique, incomplete cross-tolerance properties (81). It has been shown to restore opioid responsiveness in patients whose pain is controlled inadequately by morphine (81). Ketamine is another NMDA-receptor antagonist that has been used successfully in the ICU to reduce opioid dosages and adverse effects (82).

MYTH 7: SEDATION IS THE SAME AS ANALGESIA

A continuous sedative-hypnotic approach with benzodiazepines or propofol has historically been the first-line intervention used to provide comfort for critically ill patients receiving mechanical ventilatory support (83). However, with this approach remains the possibility that pain-induced agitation is inappropriately managed by increasing sedation, masking untreated pain. Furthermore, this approach may lead to oversedation, which occurs in 40–60% of patients despite the implementation of sedation protocols and daily sedation interruption (84, 85).

In 2007 and 2009, Payen et al (21, 85) reported results from a prospective, multicenter, observational survey of 44 French ICUs, referred to as the DOLOREA study. These reports evaluated the analgesic and sedation practices of mechanically ventilated patients during the first week of ICU stay. Importantly, results demonstrated a lack of protocolized evaluation of pain and sedation levels for patients receiving analgesics and sedation in the ICU (85). Furthermore, several improved outcomes in critically ill ventilated patients occurred when protocolized assessments were used for pain and sedation, regardless of initial analgesic and sedative strategy (21).

In addition to establishing protocolized pain and sedation assessments, increasing evidence suggests that *analgosedation*, a strategy that manages patient pain and discomfort

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first before providing sedative therapy, results in improved patient outcomes compared with standard sedative-hypnotic regimens (86). In general, a virtuous cycle occurs—adequate pain control reduces sedative and hypnotic medication dosages, decreasing sedative and hypnotic side effects and improving the ability to assess and properly manage pain. Ultimately, pain and sedation medications are used for their intended purpose, and side effects are minimized. Studies comparing analgosedation and traditional sedation regimens have reported a decreased duration of mechanical ventilation, decreased ICU length of stay, and an increase in the amount of time patients are within goal sedation ranges and pain scores (87, 88).

Among the opioids studied for the use in analgosedation, remifentanil would appear to be an attractive choice due to its high potency, fast onset, short half-life, and a metabolism independent of renal or hepatic systems (89). Remifentanil, however, is more expensive than other opioids, and hyperalgesia and opioid tolerance with administration have been reported (90). Analgosedation with morphine and fentanyl has been shown to be a safe and effective strategy to facilitate mechanical ventilation (91, 92). Given the limited data available, opioid choice should be based on patients' unique pain management needs, safety, and cost effectiveness.

Despite the benefits of the analgesia-first approach, a significant number of patients (18–70%) treated with analgesiafirst strategies will require supplementation with traditional sedative agents (89, 93, 94). One study assessed the efficacy of morphine with no sedation compared with morphine with propofol sedation; although the authors found shorter duration of ventilator days with the no sedation group, agitated delirium was higher (92). Furthermore, an increased nurse-to-patient ratio and the availability of patient "sitters" were required in one study implementing an analgosedation approach (93). Other data suggest that analgosedation does not contribute to long-term psychologic dysfunction (95).

MYTH 8: PROCEDURAL PAIN CAN BE EFFECTIVELY MANAGED AFTER THE INTERVENTION

Pain assessment before procedures has been reported to be performed only 35% of the time, and less than 25% of patients receive analgesics before procedures (86). Furthermore, preconceived ideas regarding the severity of pain seem to influence management given that medical patients receive preventive analgesia less frequently compared with surgical patients undergoing the same procedure (4).

The results of a recent prospective, multinational study reported by Puntillo et al (96) provide new insights into the prevalence, intensity, and risk factors for procedure-related pain. Data were obtained from 3,851 patients who underwent 4,812 procedures in 192 ICUs throughout 28 countries (96). An increase in pain occurred with all 12 types of procedures studied. For the three most painful procedures (chest tube removal, wound drain removal, and arterial catheter insertion), pain intensity more than doubled during the procedure compared with the preprocedural level (96). Risk factors identified to be associated with higher procedural pain included higher preprocedural pain intensity and distress, higher intensity of the worse pain on the day of the procedure, the use of opioids for the procedure, and the procedure not being performed by a nurse (96).

These results emphasize the need for increased attention to preprocedural pain assessment and sufficient preventive analgesic therapy. The preprocedural pain assessment should include the patient's current pain intensity, distress, and the "worst pain" on the day of the procedure. Paradoxically, Puntillo et al (96) found that the preemptive use of opioids was associated with greater intensity of procedural pain. This finding may reflect inadequate dosage or timing of opioid administration, suggesting that greater consideration should be given to these factors before procedures.

Although opioids are commonly used to manage procedurerelated pain, nonopioid analgesics may also be beneficial in a variety of circumstances. For example, when equianalgesic doses of ketorolac, a nonsteroidal anti-inflammatory drug, were compared with morphine for chest tube removal, both were found to be effective in minimizing pain (97). Pain caused by wound drain removal and arterial catheter insertion, the second and third most painful procedures in the study by Puntillo et al (96), can be effectively reduced by preventive local lidocaine injection (98, 99). The use of nonpharmacologic approaches, such as talking to the patient in a soothing manner, providing information about procedural details, and having family members present during the procedure, may also have a beneficial adjunctive role (100).

A striking finding of the study by Puntillo et al (96) was that across all procedures evaluated, those conducted by a nurse were associated with less pain than those conducted by other clinicians. There are several possible explanations for this finding: nurses may provide a more comfortable and reassuring environment, have a gentler approach to care, perform certain procedures better than other providers, or be more familiar with the patient's exhibited pain behavior. Although more research is needed in this area, the finding broadly supports the need for further education of pain management "best practices" for all providers in the ICU. Increased use of evidence-based guidelines, algorithms, protocols, checklists, and daily pain goals using a team-based approach will improve the consistency of pain management among providers.

MYTH 9: ELDERLY PATIENTS EXPERIENCE LESS PAIN THAN NONELDERLY PATIENTS

People who were 65 years old or older are the fastest growing segment of the population and account for 42–52% of the ICU admissions in the United States (101). The elderly frequently suffer from both acute and chronic pain–related diseases, have multiple comorbidities, and take numerous pain medications. Yet, relatively little investigative or clinical attention has been paid to the assessment and treatment of pain in the critically ill elderly population.

Clinical evidence suggests that some conditions that normally cause pain earlier in life may cause little to no pain in the elderly, for example, myocardial infarction and duodenal ulcers (102). However, experimental evidence does not support the

condition may be complicated by depression, denial, poor

health, and poor memory, all

of which impede the reporting

a heterogeneous group and

often responds differently to analgesic medications com-

pared with younger patients.

In general, the elderly popu-

lation exhibits differences in

CNS sensitivity to the effects of analgesic medications; these

patients suffer from phar-

macodynamic and pharma-

cokinetic variation affecting

medication doses and side

effects (109). Elderly patients

may require lower dosing of opioid analgesics and may have

a more rapid response to them

(106). In addition, elderly

people may develop analgesic

tolerance more slowly than

do younger individuals (110).

Because of the wide variation

of physiologic variables present between older individuals, the adage "start low and go

slow" should be applied when

initiating drug therapy.

DEVELOPMENT

OF CHRONIC PAIN

IS UNCOMMON IN SURVIVORS OF

CRITICAL ILLNESS

Pain commonly persists after

ICU discharge (111–113). The development of chronic pain (i.e., pain exceeding the aver-

age period of healing of 2-3

mo) is increasingly recognized

as a problem in survivors of

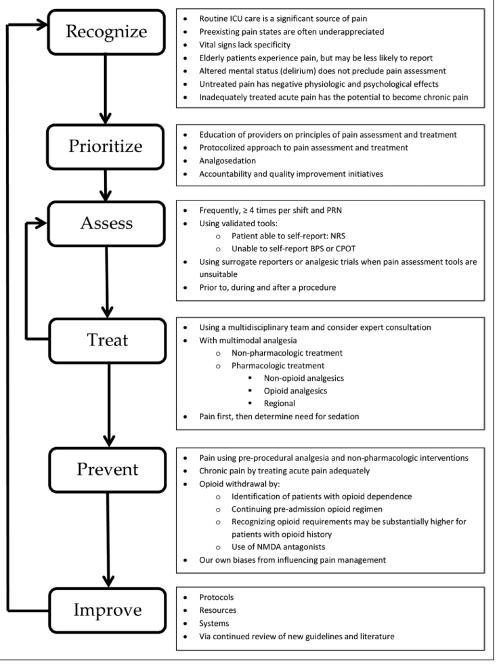
MYTH 10:

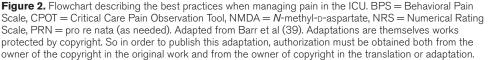
The elderly population is

commonly held belief that elderly people experience less pain than their younger counterparts. Although elderly people may have a slightly higher pain threshold (the point at which pain is first felt), they have a lower pain tolerance (the maximum pain level endured) (103, 104). In addition, there may be a difference in pain threshold depending on the type of pain inflicted. Thresholds for nonnoxious stimuli appear to increase with age, whereas pressure-pain thresholds decrease (105). Based on these differences, there is no evidence that advanced age dulls the sensation of pain.

Furthermore, pain is not an "expected and natural consequence of aging," and older people may show increased stoicism when reporting pain (106). Elderly patients may believe that pain is something to be tolerated or may be reluctant to report pain because they fear that pain is indicative of severe disease or even impending death (9, 107, 108). They may also fear the consequences of acknowledging pain, such as the need for further painful interventions, medications that have undesirable side effects, additional expenses, or further loss of independence or autonomy (107, 108). An elderly patient's

of pain.





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critical illness that negatively affects the quality of life (114). Higher rates of chronic pain have been reported in survivors of critical illness with acute respiratory distress syndrome and severe sepsis compared with a matched non-ICU population (115–117). In addition, chronic pain has been reported to be common after surgery (118).

In a study of medical and surgical ICU patients, those who recalled pain and other traumatic situations while in the ICU had a higher prevalence of chronic pain than did a comparative group of ICU patients that did not recall pain (118). Interestingly, the existence of preexisting chronic pain before ICU admission is not a consistent risk factor for chronic pain after discharge from the ICU (113).

The question of whether acute pain causes chronic pain in survivors of critical illness has not been completely resolved, but certain types of stimuli or continuous nociceptive processes provide the impetus for chronic pain to develop (112). Proinflammatory cytokine release increases pain intensity and has been suggested as a cause of chronic pain after critical illness (112). The development of chronic pain is also tissue specific, influenced by underlying genetics and mental state. Early mobilization and rehabilitation during the ICU stay may be one of the most effective strategies for reducing chronic pain and functional disability after discharge (113).

SUMMARY

Pain in critically ill patients is often underestimated, and as a result, pain management is frequently inadequate. Ongoing education is critical to overcoming barriers to adequate pain assessment and management (**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/B393). There is growing recognition that unrelieved pain is a problem that negatively affects patient outcomes. Frequent assessment using standardized validated pain assessment tools aids clinicians in individualizing treatment according to pain severity and clinical circumstances and in tailoring analgesic drug choice, dose, and dosing interval.

Appreciation of the pain associated with many commonly performed ICU procedures warrants increased attention to preprocedural pain assessment and provision of sufficient preventive analgesic therapy. An analgesic strategy that manages patient pain first before providing sedative therapy results in improved patient outcomes. Although pain control for opioidtolerant patients remains a significant challenge in the ICU, assessing a patient's baseline opioid requirement and aggressively managing acute pain appropriately—through strategies such as multimodal therapy with nonopioid medications, regional anesthetic techniques, and adequate opioid therapy will ensure adequate treatment of pain.

Chronic pain is prevalent in survivors of critical illness, and therapeutic interventions to aggressively treat acute pain and maintain mobilization may be beneficial. Engagement of a multidisciplinary team, together with a structured and ongoing commitment to process improvement in pain management, provides the best assurance that effective pain control will be achieved in the vulnerable population of the critically ill (**Fig. 2**).

REFERENCES

- Peitz GJ, Balas MC, Olsen KM, et al: Top 10 myths regarding sedation and delirium in the ICU. Crit Care Med 2013; 41:S46–S56
- Stanik-Hutt JA, Soeken KL, Belcher AE, et al: Pain experiences of traumatically injured patients in a critical care setting. *Am J Crit Care* 2001; 10:252–259
- Puntillo KA, Wild LR, Morris AB, et al: Practices and predictors of analgesic interventions for adults undergoing painful procedures. *Am J Crit Care* 2002; 11:415–429; quiz 430–431
- Chanques G, Sebbane M, Barbotte E, et al: A prospective study of pain at rest: Incidence and characteristics of an unrecognized symptom in surgical and trauma versus medical intensive care unit patients. *Anesthesiology* 2007; 107:858–860
- Grosclaude C, Asehnoune K, Demeure D, et al: [Opinion of different professional categories about the intensity of procedural pain in adult intensive care units]. Ann Fr Anesth Reanim 2010; 29:884–888
- Novaes MA, Knobel E, Bork AM, et al: Stressors in ICU: Perception of the patient, relatives and health care team. *Intensive Care Med* 1999; 25:1421–1426
- 7. Pasero C, Puntillo K, Li D, et al: Structured approaches to pain management in the ICU. *Chest* 2009; 135:1665–1672
- Tarigopula R, Tyagi NK, Jackson J, et al: Health care workers and ICU pain perceptions. *Pain Med* 2014; 15:1027–1035
- Herr KA, Garand L: Assessment and measurement of pain in older adults. Clin Geriatr Med 2001; 17:457–478, vi
- Erstad BL, Puntillo K, Gilbert HC, et al: Pain management principles in the critically ill. Chest 2009; 135:1075–1086
- 11. Cross SA: Pathophysiology of pain. Mayo Clin Proc 1994; 69:375-383
- Lindenbaum L, Milia DJ: Pain management in the ICU. Surg Clin North Am 2012; 92:1621–1636
- Akça O, Melischek M, Scheck T, et al: Postoperative pain and subcutaneous oxygen tension. *Lancet* 1999; 354:41–42
- Lewis KS, Whipple JK, Michael KA, et al: Effect of analgesic treatment on the physiological consequences of acute pain. *Am J Hosp Pharm* 1994; 51:1539–1554
- Rittner HL, Machelska H, Stein C: Leukocytes in the regulation of pain and analgesia. J Leukoc Biol 2005; 78:1215–1222
- Kyranou M, Puntillo K: The transition from acute to chronic pain: Might intensive care unit patients be at risk? Ann Intensive Care 2012; 2:36
- Granja C, Lopes A, Moreira S, et al; JMIP Study Group: Patients' recollections of experiences in the intensive care unit may affect their quality of life. *Crit Care* 2005; 9:R96–R109
- Myhren H, Ekeberg O, Tøien K, et al: Posttraumatic stress, anxiety and depression symptoms in patients during the first year post intensive care unit discharge. *Crit Care* 2010; 14:R14
- Lee YC, Lu B, Edwards RR, et al: The role of sleep problems in central pain processing in rheumatoid arthritis. *Arthritis Rheum* 2013; 65:59–68
- 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; 34:1691–1699
- Payen JF, Bosson JL, Chanques G, et al; DOLOREA Investigators: 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; 111:1308–1316
- Robinson BR, Mueller EW, Henson K, et al: An analgesia-deliriumsedation protocol for critically ill trauma patients reduces ventilator days and hospital length of stay. *J Trauma* 2008; 65:517–526
- Payen JF, Bru O, Bosson JL, et al: Assessing pain in critically ill sedated patients by using a behavioral pain scale. *Crit Care Med* 2001; 29:2258–2263
- Skrobik Y, Ahern S, Leblanc M, et al: Protocolized intensive care unit management of analgesia, sedation, and delirium improves analgesia and subsyndromal delirium rates. *Anesth Analg* 2010; 111:451–463

- Awissi DK, Bégin C, Moisan J, et al: I-SAVE study: Impact of sedation, analgesia, and delirium protocols evaluated in the intensive care unit: An economic evaluation. *Ann Pharmacother* 2012; 46:21–28
- Lattermann R, Belohlavek G, Wittmann S, et al: The anticatabolic effect of neuraxial blockade after hip surgery. *Anesth Analg* 2005; 101:1202–1208, table of contents
- Ahlers O, Nachtigall I, Lenze J, et al: Intraoperative thoracic epidural anaesthesia attenuates stress-induced immunosuppression in patients undergoing major abdominal surgery. *Br J Anaesth* 2008; 101:781–787
- Puntillo KA, Miaskowski C, Kehrle K, et al: Relationship between behavioral and physiological indicators of pain, critical care patients' self-reports of pain, and opioid administration. *Crit Care Med* 1997; 25:1159–1166
- Ahlers SJ, van Gulik L, van der Veen AM, et al: Comparison of different pain scoring systems in critically ill patients in a general ICU. *Crit Care* 2008; 12:R15
- Puntillo K, Pasero C, Li D, et al: Evaluation of pain in ICU patients. Chest 2009; 135:1069–1074
- Chanques G, Viel E, Constantin JM, et al: The measurement of pain in intensive care unit: Comparison of 5 self-report intensity scales. *Pain* 2010; 151:711–721
- Rose L, Smith O, Gelinas C, et al: Canadian critical care nurses' pain assessment and management practices: A national survey. *Am J Crit Care* 2012; 21:247–255
- 33. Gélinas C, Tousignant-Laflamme Y, Tanguay A, et al: Exploring the validity of the bispectral index, the critical-care pain observation tool and vital signs for the detection of pain in sedated and mechanically ventilated critically ill adults: A pilot study. *Intensive Crit Care Nurs* 2011; 27:46–52
- Arbour C, Gélinas C: Are vital signs valid indicators for the assessment of pain in postoperative cardiac surgery ICU adults? *Intensive Crit Care Nurs* 2010; 26:83–90
- Gélinas C, Fillion L, Puntillo KA, et al: Validation of the critical-care pain observation tool in adult patients. Am J Crit Care 2006; 15:420–427
- Chanques G, Payen JF, Mercier G, et al: Assessing pain in nonintubated critically ill patients unable to self report: An adaptation of the Behavioral Pain Scale. *Intensive Care Med* 2009; 35:2060–2067
- Gélinas C, Puntillo KA, Joffe AM, et al: A validated approach to evaluating psychometric properties of pain assessment tools for use in nonverbal critically ill adults. *Semin Respir Crit Care Med* 2013; 34:153–168
- Chanques G, Pohlman A, Kress JP, et al: Psychometric comparison of three behavioural scales for the assessment of pain in critically ill patients unable to self-report. *Crit Care* 2014; 18:R160
- 39. Barr J, Fraser GL, Puntillo K, et al; American College of Critical Care Medicine: Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013; 41:263–306
- Stites M: Observational pain scales in critically ill adults. Crit Care Nurse 2013; 33:68–78
- Odhner M, Wegman D, Freeland N, et al: Assessing pain control in nonverbal critically ill adults. *Dimens Crit Care Nurs* 2003; 22:260–267
- Voepel-Lewis T, Zanotti J, Dammeyer JA, et al: Reliability and validity of the face, legs, activity, cry, consolability behavioral tool in assessing acute pain in critically ill patients. *Am J Crit Care* 2010; 19:55–61; quiz 62
- Topolovec-Vranic J, Canzian S, Innis J, et al: Patient satisfaction and documentation of pain assessments and management after implementing the adult nonverbal pain scale. *Am J Crit Care* 2010; 19:345–354; quiz 355
- Marmo L, Fowler S: Pain assessment tool in the critically ill postopen heart surgery patient population. *Pain Manag Nurs* 2010; 11:134–140
- Topolovec-Vranic J, Gelinas C, Li Y, et al: Validation and evaluation of two observational pain assessment tools in a trauma and neurosurgical intensive care unit. *Pain Res Manag* 2013; 18:e107–e114

- 46. Azzam PN, Alam A: Pain in the ICU: A psychiatric perspective. *J Intensive Care Med* 2013; 28:140–150
- Desbiens NA, Mueller-Rizner N: How well do surrogates assess the pain of seriously ill patients? Crit Care Med 2000; 28:1347–1352
- Wibbenmeyer L, Sevier A, Liao J, et al: Evaluation of the usefulness of two established pain assessment tools in a burn population. *J Burn Care Res* 2011; 32:52–60
- Sessler CN: Progress toward eliminating inadequately managed pain in the ICU through interdisciplinary care. Chest 2009; 135:894–896
- Gordon DB, Dahl JL, Miaskowski C, et al: American Pain Society recommendations for improving the quality of acute and cancer pain management: American Pain Society Quality of Care Task Force. *Arch Intern Med* 2005; 165:1574–1580
- Upp J, Kent M, Tighe PJ: The evolution and practice of acute pain medicine. *Pain Med* 2013; 14:124–144
- 52. Erdek MA, Pronovost PJ: Improving assessment and treatment of pain in the critically ill. *Int J Qual Health Care* 2004; 16:59–64
- 53. de Jong A, Molinari N, de Lattre S, et al: Decreasing severe pain and serious adverse events while moving intensive care unit patients: A prospective interventional study (the NURSE-DO project). *Crit Care* 2013; 17:R74
- 54. Berwick DM: Developing and testing changes in delivery of care. Ann Intern Med 1998; 128:651–656
- Benyamin R, Trescot AM, Datta S, et al: Opioid complications and side effects. *Pain Physician* 2008; 11:S105–S120
- Nseir S, Hoel J, Grailles G, et al: Remifentanil discontinuation and subsequent intensive care unit-acquired infection: A cohort study. *Crit Care* 2009; 13:R60
- 57. Chang G, Chen L, Mao J: Opioid tolerance and hyperalgesia. *Med Clin North Am* 2007; 91:199–211
- Lee M, Silverman SM, Hansen H, et al: A comprehensive review of opioid-induced hyperalgesia. *Pain Physician* 2011; 14:145–161
- Malchow RJ, Black IH: The evolution of pain management in the critically ill trauma patient: Emerging concepts from the global war on terrorism. *Crit Care Med* 2008; 36:S346–S357
- Dahl JB, Kehlet H: Preventive analgesia. Curr Opin Anaesthesiol 2011; 24:331–338
- Payen JF, Genty C, Mimoz O, et al: Prescribing nonopioids in mechanically ventilated critically ill patients. J Crit Care 2013; 28: 534.e7–534.e12
- Ramaswamy S, Wilson JA, Lesley Colvin L. Non-opioid-based adjuvant analgesia in perioperative care. Cont Educ Anaesth Crit Care Pain 2013; 13:152–157
- Phillips K, Clauw DJ: Central pain mechanisms in the rheumatic diseases: Future directions. Arthritis Rheum 2013; 65:291–302
- Chanques G, Sebbane M, Constantin JM, et al: Analgesic efficacy and haemodynamic effects of nefopam in critically ill patients. *Br J Anaesth* 2011; 106:336–343
- 65. Hebl JR, Niesen AD: Infectious complications of regional anesthesia. *Curr Opin Anaesthesiol* 2011; 24:573–580
- Stundner O, Memtsoudis SG: Regional anesthesia and analgesia in critically ill patients: A systematic review. *Reg Anesth Pain Med* 2012; 37:537–544
- 67. Capdevila X, Pirat P, Bringuier S, et al; French Study Group on Continuous Peripheral Nerve Blocks: Continuous peripheral nerve blocks in hospital wards after orthopedic surgery: A multicenter prospective analysis of the quality of postoperative analgesia and complications in 1,416 patients. *Anesthesiology* 2005; 103:1035–1045
- Madsen MV, Gøtzsche PC, Hróbjartsson A: Acupuncture treatment for pain: Systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. *BMJ* 2009; 338:a3115
- Gorji HM, Nesami BM, Ayyasi M, et al: Comparison of ice packs application and relaxation therapy in pain reduction during chest tube removal following cardiac surgery. N Am J Med Sci 2014; 6:19–24
- Gélinas C, Arbour C, Michaud C, et al: Patients and ICU nurses' perspectives of non-pharmacological interventions for pain management. *Nurs Crit Care* 2013; 18:307–318

Critical Care Medicine

www.ccmjournal.org 2477

- Friesner SA, Curry DM, Moddeman GR: Comparison of two painmanagement strategies during chest tube removal: Relaxation exercise with opioids and opioids alone. *Heart Lung* 2006; 35:269–276
- 72. Cepeda MS, Carr DB, Lau J, et al: Music for pain relief. *Cochrane Database Syst Rev* 2006; 2:CD004843
- Cohen SP, Christo PJ, Wang S, et al: The effect of opioid dose and treatment duration on the perception of a painful standardized clinical stimulus. *Reg Anesth Pain Med* 2008; 33:199–206
- Doverty M, Somogyi AA, White JM, et al: Methadone maintenance patients are cross-tolerant to the antinociceptive effects of morphine. *Pain* 2001; 93:155–163
- Nalamachu SR: Opioid rotation in clinical practice. Adv Ther 2012; 29:849–863
- Mitra S, Sinatra RS: Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology* 2004; 101:212–227
- Alford DP, Compton P, Samet JH: Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med* 2006; 144:127–134
- Fine PG, Portenoy RK; Ad Hoc Expert Panel on Evidence Review and Guidelines for Opioid Rotation: Establishing "best practices" for opioid rotation: Conclusions of an expert panel. J Pain Symptom Manage 2009; 38:418–425
- Silverman SM: Opioid induced hyperalgesia: Clinical implications for the pain practitioner. *Pain Physician* 2009; 12:679–684
- Mehta V, Langford RM: Acute pain management for opioid dependent patients. Anaesthesia 2006; 61:269–276
- Prommer E: Rotating methadone to other opioids: A lesson in the mechanisms of opioid tolerance and opioid-induced pain. J Palliat Med 2006; 9:488–493
- De Pinto M, Jelacic J, Edwards WT: Very-low-dose ketamine for the management of pain and sedation in the ICU. J Opioid Manag 2008; 4:54–56
- Wunsch H, Kahn JM, Kramer AA, et al: Use of intravenous infusion sedation among mechanically ventilated patients in the United States. *Crit Care Med* 2009; 37:3031–3039
- Jackson DL, Proudfoot CW, Cann KF, et al: The incidence of suboptimal sedation in the ICU: A systematic review. *Crit Care* 2009; 13:R204
- Payen JF, Chanques G, Mantz J, et al: Current practices in sedation and analgesia for mechanically ventilated critically ill patients: A prospective multicenter patient-based study. *Anesthesiology* 2007; 106:687–695; quiz 891–892
- Bevabhakthuni S, Armahizer MJ, Dasta JF, et al: Analgosedation: A paradigm shift in intensive care unit sedation practice. Ann Pharmacother 2012; 46:530–540
- 87. Karabinis A, Mandragos K, Stergiopoulos S, et al: Safety and efficacy of analgesia-based sedation with remifentanil versus standard hypnotic based regimens in intensive care unit patients with brain injuries: A randomised, controlled trial. *Crit Care* 2004; 8:R268–R280
- Breen D, Karabinis A, Malbrain M, et al: Decreased duration of mechanical ventilation when comparing analgesia-based sedation using remifentanil with standard hypnotic-based sedation for up to 10 days in intensive care unit patients: A randomised trial [ISRCTN47583497]. *Crit Care* 2005; 9:R200–R210
- Wilhelm W, Kreuer S: The place for short-acting opioids: Special emphasis on remifentanil. *Crit Care* 2008; 12(Suppl 3):S5
- Kim SH, Stoicea N, Soghomonyan S, et al: Intraoperative use of remifentanil and opioid induced hyperalgesia/acute opioid tolerance: Systematic review. *Front Pharmacol* 2014; 5:108
- Tedders KM, McNorton KN, Edwin SB: Efficacy and safety of analgosedation with fentanyl compared with traditional sedation with propofol. *Pharmacotherapy* 2014; 34:643–647
- Strøm T, Martinussen T, Toft P: A protocol of no sedation for critically ill patients receiving mechanical ventilation: A randomised trial. *Lancet* 2010; 375:475–480
- Park G, Lane M, Rogers S, et al: A comparison of hypnotic and analgesic based sedation in a general intensive care unit. *Br J Anaesth* 2007; 98:76–82

- 94. Rozendaal FW, Spronk PE, Snellen FF, et al; UltiSAFE Investigators: Remifentanil-propofol analgo-sedation shortens duration of ventilation and length of ICU stay compared to a conventional regimen: A centre randomised, cross-over, open-label study in the Netherlands. *Intensive Care Med* 2009; 35:291–298
- Strøm T, Stylsvig M, Toft P: Long-term psychological effects of a nosedation protocol in critically ill patients. *Crit Care* 2011; 15:R293
- Puntillo KA, Max A, Timsit JF, et al: Determinants of procedural pain intensity in the intensive care unit. The Europain® study. Am J Respir Crit Care Med 2014; 189:39–47
- Puntillo K, Ley SJ: Appropriately timed analgesics control pain due to chest tube removal. Am J Crit Care 2004; 13:292–301; discussion 302; quiz 303–304
- Yiannakopoulos CK, Kanellopoulos AD: Innoxious removal of suction drains. Orthopedics 2004; 27:412–414
- 99. Lightowler JV, Elliott MW: Local anaesthetic infiltration prior to arterial puncture for blood gas analysis: A survey of current practice and a randomised double blind placebo controlled trial. J R Coll Physicians Lond 1997; 31:645–646
- Faigeles B, Howie-Esquivel J, Miaskowski C, et al: Predictors and use of nonpharmacologic interventions for procedural pain associated with turning among hospitalized adults. *Pain Manag Nurs* 2013; 14:85–93
- 101. Pisani MA: Considerations in caring for the critically ill older patient. J Intensive Care Med 2009; 24:83–95
- Rosenthal RA, Kavic SM: Assessment and management of the geriatric patient. Crit Care Med 2004; 32:S92–S105
- 103. Gibson SJ: Progress in pain research and management. In: Proceedings of the 10th World Congress on Pain. Vol. 24. Dostrovsky JO, Carr DB, Kaltenzburg M (Eds). Seattle, WA, IASP Press, 2003, pp 767–790
- 104. McCleane G: Pharmacological pain management in the elderly patient. Clin Interv Aging 2007; 2:637–643
- Lautenbacher S, Kunz M, Strate P, et al: Age effects on pain thresholds, temporal summation and spatial summation of heat and pressure pain. *Pain* 2005; 115:410–418
- Hadjistavropoulos T, Herr K, Turk DC, et al: An interdisciplinary expert consensus statement on assessment of pain in older persons. *Clin J Pain* 2007; 23:S1–S43
- 107. Hofland SL: Elder beliefs: Blocks to pain management. J Gerontol Nurs 1992; 18:19–23
- 108. Portenoy RK, Farkash A: Practical management of non-malignant pain in the elderly. *Geriatrics* 1988; 43:29–40, 44–47
- 109. Coldrey JC, Upton RN, Macintyre PE: Advances in analgesia in the older patient. Best Pract Res Clin Anaesthesiol 2011; 25:367–378
- Bontin-Mushock C, Philip L, Moriyama K, et al: Age dependent opioid escalation in chronic pain patients. *Anesth Analg* 2005; 100:1740–1745
- 111. Schelling G, Stoll C, Haller M, et al: Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. *Crit Care Med* 1998; 26:651–659
- 112. Voscopoulos C, Lema M: When does acute pain become chronic? Br J Anaesth 2010; 105(Suppl 1):i69–i85
- 113. Adler J, Malone D: Early mobilization in the intensive care unit: A systematic review. *Cardiopulm Phys Ther J* 2012; 23:5–13
- 114. García Lizana F, Peres Bota D, De Cubber M, et al: Long-term outcome in ICU patients: What about quality of life? *Intensive Care Med* 2003; 29:1286–1293
- 115. Dowdy DW, Eid MP, Dennison CR, et al: Quality of life after acute respiratory distress syndrome: A meta-analysis. *Intensive Care Med* 2006; 32:1115–1124
- 116. Zimmer A, Rothaug J, Mescha S, et al: Chronic pain after surviving sepsis. *Crit Care* 2006; 10:421
- 117. Battle CE, Lovett S, Hutchings H: Chronic pain in survivors of critical illness: A retrospective analysis of incidence and risk factors. *Crit Care* 2013; 17:R101
- 118. Perkins FM, Kehlet H: Chronic pain as an outcome of surgery. A review of predictive factors. *Anesthesiology* 2000; 93:1123–1133

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