Improving outcomes in med-surg patients with opioid-induced respiratory depression

Myth debunking and better recognition of respiratory compromise can help prevent deaths.

By Frank J. Overdyk, MSEE, MD, and Jesse J. Guerra, MSN, RN-BC

EVERY YEAR, from 350,000 to 750,000 in-hospital cardiopulmonary arrests (IHCAs) occur in the United States. About 80% of the victims don't survive to discharge; among those who do, some suffer permanent anoxic brain injury. Patient outcomes haven't improved measurably in 40 years.

Studies show roughly half of patients with IHCAs had been receiving opioids. Opioid-induced respiratory depression (OIRD) has an insidious progression. Hard to diagnose, it's likely to lead to death or anoxic brain injury unless detected promptly. Outcomes are worse when IHCA occurs at night or on the weekend, when staffing levels and patient interaction are lowest.

Two leading factors influence IHCA outcomes—whether the event was witnessed and how soon cardiopulmonary resuscitation (CPR) begins. In intensive care units (ICUs) and emergency departments (EDs), IHCAs typically are witnessed, and responders and equipment are available immediately to start CPR. But on med-surg units, patients' vital signs may be taken only every 4 hours and rapid response teams (RRTs) have to be summoned from remote locations. Although estimates of OIRD incidence among postsurgical med-surg patients range from 0.5% to 2%, a study using continuous pulse oximetry and end-tidal carbon dioxide ($EtCo_2$) monitoring suggests OIRD is much more common among this population.

The truth about IHCA

Many healthcare providers assume IHCA correlates with chronic advanced disease states and advanced age. Yet IHCA victims have a low prearrest morbidity score—a measure of the degree of sickness. What's more, their average age is only 57 and their median hospital stay is 3 days.

IHCA resuscitation studies have shed light on the common causes and time course of the pathophysiologic deterioration that precedes an IHCA. A detailed review of 139 in-hospital deaths found IHCAs were potentially avoidable in 62% of cases, and clinical signs of deterioration went unattended in 48% of cases. Also, med-surg patients were five times more likely to suffer avoidable IHCAs than ICU patients and accounted for nearly two-thirds of hospital deaths.

Why respiratory monitoring is crucial

Historically, hemodynamic monitoring (blood pressure, heart rate, and heart rhythm) has taken center stage in bedside patient assessment. To reduce the risk of unexpected and unrecognized cardiac arrhythmias, hospitals have established cardiac telemetry units for continuous remote monitoring of patients at risk for rhythm disturbances.

Yet the most common events preceding IHCAs are *respiratory*—not arrhythmias or hemodynamic disturbances. Typically, the earliest warning signs of physiologic instability reflect respiratory decompensation—tachypnea, bradypnea, hypoxia, hypercarbia, and mental status changes. Monitoring of respiratory function and level of con-

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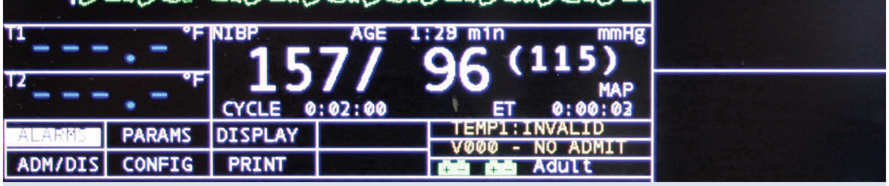
LEARNING OBJECTIVES

1. Explain how to assess patients for opioid-induced respiratory depression.
2. State myths related to opioid use in patients with chronic pain.
3. Identify variations in individuals' response to opioids.

The planners of this CNE activity have disclosed no relevant financial relationships with any commercial companies pertaining to this activity. Author Frank J. Overdyk has been a speaker and consultant for Covidien and CareFusion; author Jesse Guerra works for CareFusion. The content of this CNE activity was peer-reviewed for bias, and none was found. See the last page of the article to learn how to earn CE credit.



Are RRT triggers appropriate?

The rapid response system (RRS) was developed in the early 1990s in recognition that specific abnormal vital signs and symptoms precede in-hospital cardiopulmonary arrest. Timely detecting of these signs and symptoms promotes interventions that preempt the decompensation leading to cardiopulmonary arrest. Yet use of the RRS and rapid response teams (RRTs) hasn't consistently reduced adjusted hospital mortality—in part due to clinicians' knowledge gaps and deficiencies in current standards for respiratory and central nervous system monitoring on medical-surgical units.

Two of the four components of the RRS—the afferent and efferent limbs—are critical to its success.

- The *afferent* limb includes the clinical staff and bedside monitors that can *detect* early signs and symptoms of decompensation, as defined by the staff's clinical trigger criteria.
- The *efferent* limb includes the clinical staff (medical emergency team and RRT), monitors, and equipment that *respond* to a trigger event.

Although RRS implementation has reduced both the incidence of "code blue" calls and raw mortality in many hospitals, debate lingers on whether it's universally effective in reducing adjusted mortality and improving outcomes. A persistent weakness of the RRS construct is the set of triggers in the afferent limb, which bedside providers use to raise the alarm; most of these triggers (such as respiratory rate and peripheral oxygen saturation) rely on manual and intermittent vital-sign measurements.

sciousness (LOC) is especially crucial in preventing adverse events in med-surg patients receiving opioids and sedatives. Unfortunately, few hospitals have the capacity to monitor these indices remotely and continuously, except in ICU or step-down settings.

Evaluating for OIRD warning signs

Many clinicians mistakenly focus on the respiratory rate (RR) when assessing patients for OIRD. But evaluating LOC is more likely to uncover warning signs of OIRD.

> *Fiction:* A slow RR (less than 8 breaths per minute [bpm], or bradypnea) is the most important and sensitive vital-sign warning of OIRD.
>
> *Quote:* "The patient can't possibly have had a respiratory arrest. In the 2 hours before the code, his charted respiratory rates were 16 and 12." (*Note:* This quote and the other quotes in this article are actual clinician statements.)
>
> *Fact:* Although opioids commonly cause bradypnea, *absence* of bradypnea doesn't rule out respiratory depression. Reduced LOC, not a slow RR, is the clinical finding with the best chance of not missing OIRD detection.

The Pasero Opioid-Induced Sedation Scale (POSS) was designed specifically to assess opioid-induced mental status changes. A survey-based study found POSS demonstrated adequate measures of reliability and validity in measuring sedation during opioid administration for pain management. It also found POSS has clinical significance in determining the accuracy of clinical assessments and subsequent actions for patients experiencing advancing sedation during opioid analgesia. But no sedation scale is specific for opioid-induced sedation, so clinicians should consider other diagnoses once opioid overdose is ruled out.

Pitfalls in measuring and interpreting RR and LOC

Not only is RR a poor measure of overall respiratory function, but manual RR measurement is the most difficult bedside vital-sign measurement to take and in many cases is inaccurate. An accurate RR measurement requires a prolonged sampling period and careful attention to detail, including observation of breathing depth and pauses. A respiratory hallmark in patients receiving opioids is irregular breathing, not just slow breathing.

Thus, measuring RR over 30 seconds may yield a false-low or false-high result. Triggers for summoning the RRT commonly are set at an absolute threshold of 8 bpm or less for bradypnea and 90% or less for peripheral oxygen saturation (Spo_2). Consequently, clinicians may misinterpret the patient's respiratory status and take inappropriate measures, as described in the clinical examples that follow.

Clinical example A

Although the patient's RR is measured at 8 bpm, he's taking markedly deep breaths. He rates his pain as 2 on a scale of 0 to 10, and is awake and oriented to person, place, and time. The nurse lengthens the lockout interval on the patient-controlled analgesia (PCA) pump to prevent further RR slowing.

Explanation: A slow RR is a normal physiologic response to opioids. An RR of 8 bpm may not warrant intervention if the patient is awake, appropriate, and comfortable. In this case, backing off the PCA opioid regimen is inappropriate, as it may exacerbate the patient's pain. And calling the RRT based on a breach of the RR threshold of 8 bpm would constitute a false alarm. Instead, the nurse should identify and grade changes in the patient's sedation level and respiratory quality, including changes in respiratory pattern and depth and noisy breathing. (See *Are RRT triggers appropriate?*)

Clinical example B

The patient is breathing at 12 to 15

Stay alert for false-negatives

Data from continuously monitored med-surg patients show increased end-tidal carbon dioxide ($EtCO_2$) values caused by respiratory depression—yet their respiratory rates (RRs) and peripheral oxygen saturation (SpO_2) values wouldn't trigger a rapid response team alert with alarm thresholds of an RR of 8 breaths/minute or lower and SpO_2 values below 90%. Data in this table derive from a study showing respiratory depression in different patients with normal SpO_2 values.

Respiratory rate (breaths/minute)	$EtCO_2$ average (mm Hg)	SpO_2 average
14	65	96%
18	57	96%
11	57	94%
12	68	95%
16	58	96%
11	56	99%
11	56	98%
10	57	100%
13	56	100%
13	70	96%

Source: Overdyk F, Carter R, Maddox R, et al. Continuous oximetry/capnometry monitoring reveals frequent desaturation and bradypnea during patient-controlled analgesia. *Anesth Analg*. 2007 Aug;105(2):412-8.

bpm but is lethargic and complains of 8/10 pain when aroused. A spot SpO_2 value of 95% is measured with a bedside oximeter.

Explanation: This scenario was replicated multiple times in a study measuring continuous oximetry and capnography in patients receiving PCA. The study found patients had significant clinical respiratory depression with end-tidal capnography values above 55 mm Hg. Their sedation stemmed from hypercarbia, yet their SpO_2 values remained normal—even though not all of the patients were receiving supplemental oxygen by nasal cannula. In these cases, the RRT respiratory triggers of an RR of 8 bpm or lower and SpO_2 below 90% were falsely negative, and the patients could have suffered respiratory arrest. (See *Stay alert for false-negatives*.)

Clincial example C

At 4 A.M., your patient is curled up under the bedcovers and snoring lightly as you perform a routine bedside assessment. When you awaken her to evaluate her pain and sedation levels, you find her slow to arouse, disoriented, and speaking incoherently. She falls asleep during your assessment; you measure an RR of 10 bpm and note that her PCA button was last pressed at 2 A.M.

Explanation: This scenario highlights the difficulty of patient assessment during the early morning hours. The patient's disorientation may stem from being awakened from slow-wave or rapid-eye-movement (REM) sleep—or she might be hypercarbic and have significant respiratory depression. The two conditions can't be differentiated without more extensive investigation, which may be impractical and is often avoided at this hour. Yet, most catastrophic outcomes from unrecognized respiratory depression occur in the early morning.

Understanding the variable effects of opioids

Various factors influence the safety with which opioids can be given postoperatively. Because the effects of a given opioid dosage may vary greatly among patients, dosages must be individualized. (See *Factors influencing opioid effects.*)

Fiction: A standard dosage of an opioid is always safe.

Quote: "This patient can't have had a respiratory arrest because he was getting a standard morphine dosage by PCA."

Fact: There's no standard opioid dosage that guarantees a patient will avoid respiratory depression; there's only a *starting* dosage. The only way to ensure a safe and effective opioid-based analgesic regimen is to carefully and frequently titrate the starting-dose regimen (including PCA) to the patient's pain and sedation scores and to assess vital signs frequently.

Analgesic variability results from differences in both pharmacokinetics (relationship between drug dose and drug blood level) and pharmacodynamics (relationship between drug blood level and drug effect) among patients. Examples of pharmacokinetic and pharmacodynamic factors include the following:

- *Gender:* Morphine has a slower analgesic onset (pharmacokinetic factor) in women than in men, but is more potent in women (pharmacodynamic factor).
- *Genetics:* The mu-opioid receptor (MOR) has genetic variability (polymorphism), which means patients differ in morphine sensitivity depending on their genetic makeup.
- *Drug interactions:* Residual intraoperative anesthetics, sedatives, and opioids act synergistically or additively with opioids' sedative and respiratory depressant effects postoperatively.
- *Comorbidities:* Sleep apnea and certain other conditions predispose patients to airway collapse; also, liver and kidney failure affect metabolism and excretion of opioids and their active metabolites.
- *Sleep and diurnal rhythms:* Transient airway collapse is the hallmark of obstructive sleep apnea

Factors influencing opioid effects

This table lists factors that contribute to the wide variability in opioid effects among patients.

Factor	Examples
Age	Increased age has a linear correlation to increased opioid sensitivity. Thus, elderly patients require lower opioid dosages than younger patients to experience the same analgesic effect.
Circadian rhythm and sleep stage	Slow-wave and rapid-eye-movement sleep reduce airway patency.
Comorbidities	Patients with renal or hepatic disease may have decreases in the metabolism or elimination of opioids or their active metabolites. Also, patients with obstructive sleep apnea or chronic pain syndromes are susceptible to airway collapse or altered respiratory drive.
Drug interactions	Drugs with sedative properties (such as sleeping pills, muscle relaxants, and psychotropics) interact synergistically with opioids to worsen respiratory depression. Antibiotics and certain other drugs may impede opioid metabolism or excretion.
Gender	Women respond more slowly to opioids but are more sensitive to their effects. They require longer dosing intervals.
Genomics	Differences in genetic makeup account for marked differences in analgesic effect among patients receiving the same opioid dosage.
Pain level	As pain level decreases, respiratory drive and airway patency decline.

(OSA). Yet anesthetics and sedatives produce similar effects in patients without OSA. Thus, all postoperative patients (who typically experience sleep deprivation and REM-sleep rebound) are at risk for unpredictable episodes of airway obstruction, especially at night.

- *Pain level:* Pain stimulates the respiratory centers and promotes airway patency. Fluctuations in pain levels due to intermittent opioid dosing or regional anesthesia cause fluctuations in respiratory depression.

Postoperative management of patients with chronic pain

The population of surgical patients taking long-term opioids is rising rapidly. Twelve million people in the United States took opioids for nonmedical reasons in 2007. Many more took them for chronic pain syndromes.

Postoperative patients on long-term opioid therapy need the same meticulous monitoring for drug side effects as opioid-naïve patients. Respiratory depression remains a prominent cause of death in opioid-addicted individuals and in patients receiving intrathecal opioids for chronic pain syndromes.

Postoperative patients with chronic pain are unlikely to experience significant respiratory depression after receiving starting opioid dosages typically given to opioid-naïve patients. But these patients rarely receive those opioid dosages, because their opioid tolerance and opioid-induced hyperalgesia mean that providers must rapidly escalate therapy to higher dosages and use multimodal opioid analgesics (such as I.V. or transdermal administration) to meet pain treatment guidelines. At these higher dosages, chronic-pain patients are susceptible to respiratory depression.

Fiction: Patients on long-term opioid therapy are less likely than opioid-naïve patients to suffer respiratory depression from postoperative opioids.

Quote: "Ms. Caldwell took a lot of pain pills at home. There's no way she can go into respiratory arrest while using PCA."

Fact: Patients on long-term opioid therapy have higher opioid requirements for adequate pain relief. At these higher dosages, they're just as susceptible to respiratory depression as opioid-naïve patients are at lower dosages. Also, patients on long-term opioids have baseline respiratory abnormalities—specifically, increased periods of central apnea and ataxic breathing—which opioids and sedatives may exacerbate postoperatively.

Fiction: A patient with a high pain level can't experience respiratory depression.

Fact: Although pain stimulates respiratory centers and promotes airway patency, recent studies suggest respiratory depression can occur without adequate analgesia; high plasma morphine levels causing respiratory depression don't correlate with low pain scores. Further clinical and laboratory assessment may be needed to determine appropriate interventions in this difficult scenario.

Fiction: Some opioids don't cause respiratory depression.

Fact: Opioids' analgesic and respiratory depressant effects are inalterably linked at a common locus—the MOR. Extensive research on alternative opioid ligands and receptors has failed to find an analgesic opioid that doesn't depress respiratory drive. The most effective way to prevent respiratory depression is to use opioid-sparing analgesic agents in combination with opioids to reduce the required opioid dosage. Examples of these agents include local anesthetics, nonsteroidal drugs, cyclooxygenase-2 inhibitors, ketamine, gabapentin, partial opioid agonist-antagonists, and even chili peppers. Other opioid-sparing modalities include regional postoperative pain therapies, transcutaneous nerve stimulation, and transcranial magnetic stimulation.

What the future may hold

Respiratory decompensation on med-surg units is likely to become more common as the demographic of surgical patients shifts towards older and more overweight individuals. What's more, intermittent airway obstruction and central apnea are common in patients who've received general anesthesia—and will grow more prevalent with the expanding population of patients who have sleep-disordered breathing and OSA.

Most clinicians acknowledge that unrecognized adverse respiratory events in patients receiving opioids stem largely from the intermittent nature of bedside monitoring. Various strategies are being used in response to such deficiencies. The most recent guidelines from the definitive nursing text on bedside monitoring for patients on opioids recommend a much shorter interval between bedside vital-sign assessments, despite the extra burden this imposes on staff. Some healthcare systems have implemented continuous respiratory monitoring of SpO_2, $EtCO_2$, or both on med-surg units (with or without telemetry)—with satisfactory results. A recent study suggests centrally monitored continuous oximetry with wireless provider notification may reduce RRT calls and transfers to the ICU.

However, according to the Consensus Conference on Medical Emergency Teams, recommending this technology would be premature because of the high false-positive rate and associated costs and workflow disruption of continuous respiratory monitoring equipment. Promising new developments in monitoring and alarm technology are improving specificity (resulting in fewer false-positives) without compromising sensitivity by increasing false-negatives. Monitors will include smaller body-borne wireless sensors that yield higher-resolution data with better motion detection and artifact rejection. Monitors will no longer use simple arbitrary thresholds of a single parameter, such as heart rate or SpO_2, to trigger an alarm. Instead, they'll fuse multiple vital signs into heuristic algorithms that interpret the whole clinical picture, much like a clinician would do at the bedside.

OIRD and IHCA result in more serious adverse events for med-surg patients than for patients in ICUs and EDs—monitored settings where arrests are likely to be witnessed and therapeutic interventions can begin at once. Early recognition of respiratory compromise and timely intervention through improved monitoring, staffing levels, and resources are urgently needed to improve the tragic and preventable illnesses and deaths from OIRDs and IHCAs among med-surg patients. ✯

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Purpose/Goal

To enhance medical-surgical nurses' understanding of opioid-induced respiratory depression

Learning Objectives

1. Explain how to assess patients for opioid-induced respiratory depression.
2. State myths related to opioid use in patients with chronic pain.
3. Identify variations in individuals' response to opioids.

Please mark the correct answer online.

1. Which statement about med-surg patients and in-hospital cardiac arrest (IHCA) is correct?
a. Med-surg patients are less likely than intensive care unit (ICU) patients to suffer avoidable IHCAs.
b. Med-surg patients are more likely than ICU patients to suffer avoidable IHCAs.
c. IHCA victims have a high morbidity score.
d. IHCA victims' average age is 72.

2. The most common events preceding IHCAs are:
a. respiratory related.
b. arrhythmias.
c. related to hemodynamic changes.
d. related to tachycardia episodes.

3. Which statement about assessing respiratory rate and opioid-induced respiratory depression (OIRD) is correct?
a. It's easy to obtain an accurate respiratory rate (RR) manually.
b. Absence of bradypnea rules out respiratory depression.
c. Evaluating level of consciousness (LOC) is more likely than RR assessment to uncover OIRD warning signs.
d. RR assessment is more likely than LOC evaluation to uncover OIRD warning signs.

4. Which statement about a study of patients with significant respiratory depression and end-tidal carbon dioxide values above 55 mm Hg is accurate?
a. Their peripheral oxygen saturation (Spo_2) values remained normal.
b. Their Spo_2 values increased significantly.
c. Their Spo_2 values increased slightly.
d. Their Spo_2 values decreased by 50%.

5. Using a standard opioid dosage:
a. is the safest way to set dosages for patients.
b. will guarantee that the patient will avoid respiratory depression.
c. won't guarantee that the patient will avoid respiratory depression.
d. is recommended for all patients.

6. Which statement about analgesic variability is correct?
a. The xu-opioid receptor affects morphine sensitivity.
b. The mu-opioid receptor doesn't affect morphine sensitivity.
c. Morphine has a slower analgesic onset in men than in women.
d. Morphine has a slower analgesic onset in women than in men.

7. For postoperative patients with chronic pain:
a. opioid dosages usually given to opioid-naïve patients rarely cause serious respiratory depression.
b. opioid dosages usually given to opioid-naïve patients commonly cause serious respiratory depression.
c. rapid escalation of opioid dosages doesn't make patients susceptible to respiratory depression.
d. rapid escalation of opioid dosages shouldn't be used for patients with chronic pain.

8. Your postoperative patient has a history of chronic pain. When monitoring her respiratory status, you should keep in mind that:
a. high levels of morphine causing respiratory depression correlate with low pain scores.
b. respiratory depression can occur in patients with a high pain level.
c. patients with a high pain level can't experience respiratory depression.
d. some opioids don't cause respiratory depression.

9. Which of the following is *not* an opioid-sparing analgesic agent?
a. Morphine
b. Chili peppers
c. Ketamine
d. Gabapentin

10. The efferent limb of the rapid response system (RRS) includes:
a. RR assessment used in response to decompensation.
b. equipment used to detect a trigger event.
c. clinical staff who respond to a trigger event.
d. clinical staff who detect early signs of decompensation.

11. Which statement accurately indicates how sleep can influence opioid effect?
a. Slow-wave sleep reduces airway patency.
b. Rapid-eye-movement sleep increases airway patency.
c. Rapid-wave movement reduces airway patency.
d. Slow-eye-movement sleep reduces airway patency.

12. For elderly patients recovering from surgery, you should anticipate which of the following?
a. They will require higher opioid dosages than younger patients to experience the same analgesic effect.
b. They will require lower opioid dosages than younger patients to experience the same analgesic effect.
c. They will require longer opioid dosing intervals and will respond more slowly to opioids.
d. They are likely to have differences in genetic makeup that affect opioid response.

13. Patients on long-term opioids have baseline respiratory abnormalities that opioids and sedatives may exacerbate postoperatively, such as:
a. syntaxic breathing.
b. ataxic breathing.
c. reduced periods of central apnea.
d. increased periods of peripheral apnea.

14. Which statement about continuous bedside monitoring on med-surg units is true?
a. The Consensus Conference on Medical Emergency Teams recommends this technology for med-surg units.
b. The Consensus Conference on Medical Emergency Teams recommends this technology in orthopedic units.
c. Centrally monitored continuous oximetry with provider notification has no effect on rapid response calls.
d. Centrally monitored continuous oximetry with provider notification may reduce rapid response calls.

15. The Pasero Opioid-Induced Sedation Scale:
a. can be used to assess opioid-induced mental status changes.
b. can be used to assess opioid-induced physical status changes.
c. has insufficient validity for clinical use.
d. has insufficient reliability for clinical use.