automated and continuous vital sign measurements, are prone to undersampling, and are likely underpowered to "connect the dots" with regard to the outcomes in the resuscitation literature.

Our failure on the GCF is not one of “rescue” but of “recognition.” OIRD is a preventable adverse event, and 78% of cardiac arrests on the GCF are deemed avoidable in root cause analysis. The odds of a potentially avoidable cardiac arrest were five times higher on the GCF than in an intensive care setting, and outcomes are worst during periods of decreased vigilance, such as nights and weekends. Recent vital signs, such as a respiratory rate, are missing in as many as 75% of patients for whom a Code Blue or a rapid response team is summoned.

The Anesthesia Patient Safety Foundation convened a symposium in 2006 on the dangers of postoperative opioids, and the consensus opinion was that OIRD remains a significant and preventable threat to patient safety for which institutions must have zero tolerance. In recognition of the gravity of the problem, the 2011 edition of a preeminent nursing text on monitoring patients on opioids recommends that the monitoring interval for vital signs GCF could be greatly reduced, despite the additional burden imposed on the GCF nursing staff.

Three demographic trends are likely to make OIRD more prevalent in the future. The population is aging and obesity is more common, both of which predispose patients to obstructive sleep apnea. Recurrent airway obstruction due to opioid-mediated suppression of the arousal response and the upper airway dilators is the predominant feature of respiratory compromise in postoperative patients with obstructive sleep apnea. Chronic opioid use for both medical and nonmedical reasons is escalating, and these patients are predisposed to have ataxic breathing patterns and frequent central apneas. This predisposition in combination with the higher opioid doses and multimodal opioid therapy they require for adequate pain relief places them at an increased risk of respiratory compromise. Yet, the irregular breathing patterns and transient desaturations that precede respiratory decompensation in these patients are unlikely to be detected by intermittent respiratory rate and \( \text{SpO}_2 \) measurements.

Improved understanding by clinicians of the complex pharmacologic nuances of opioids and expanded use of multimodal, opioid-sparing analgesic techniques are important contributors to reducing OIRD. But recognition of the scope of OIRD and improving its detection remain pressing unresolved issues in postoperative pain management.

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**References**


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**In Reply:**

We thank Dr. Overdyk for his interest in our review article. In his letter, Dr. Overdyk addresses the issue of incidence and detection of opioid-induced respiratory depression. Although the focus of our review was on rescue, treatment (with naloxone and alternative agents), and prevention, rather than recognition, we agree with Dr. Overdyk that the incidence of opioid-induced respiratory depression may be underreported, especially in certain high-risk populations. We report from the literature an incidence of opioid-induced respiratory depression that requires direct intervention between one in 200 and one in 50 in American Society of Anesthesiologists I and II patients. These data compare with the incidence of opioid-induced respiratory depression that we encounter in our academic institution in which pain

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treatment is determined and closely monitored by anesthesiologists as a part of an acute pain service. We can accept that under circumstances in which pain treatment and the monitoring of patients are not closely controlled by anesthesiologists or an acute pain service, the incidence of opioid-induced respiratory depression is higher.

We agree that, in patients with specific characteristics, the incidence of respiratory events after opioid treatment may also be higher, for example, in severely ill or aged patients, the morbidly obese, patients with specific underlying diseases (e.g., diseases of the lungs or the respiratory muscles), and patients with obstructive sleep apnea. However, estimations of morbidity and mortality from opioid administration are not easily available for these specific patient populations for various reasons. In some cases (e.g., in severely ill or extremely old patients), the occurrence of respiratory arrest is sometimes assumed to be related to the underlying disease and old age rather than to the intervention. In other cases, as indicated by Dr. Overdyk, relevant measures of respiratory depression are just not given, and we remain uninformed on the cause of respiratory arrest. As we state in our article, respiratory frequency and oxygen–hemoglobin saturation are not direct measures of opioid-induced respiratory effect. Severe opioid-induced respiratory depression (such as that may occur after an overdose) is characterized by an initial period of irregular breathing without affecting respiratory rate, but with an increase in arterial carbon dioxide concentration, followed by a period of cyclic breathing, and finally by bradypnea and respiratory arrest (apneic). Simply monitoring respiratory frequency and oxygen–hemoglobin saturation may miss the initial phases of opioid-induced respiratory depression. The ensuing bradypnea and respiratory arrest may come so quickly that adequate treatment may be late, sometimes too late. Therefore, monitoring of patients at risk for respiratory depression that still require opioid treatment is best suited to a special ward (medium- or high-care units) with close monitoring of not only vital signs that include arterial or end-tidal carbon dioxide but also electrocardiogram and heart rate. Tachycardia and arrhythmias may be among the first signs of extreme hypercapnia even when the oxygen–hemoglobin concentration is still in the normal range. Interestingly, a recent study on the implementation of a patient surveillance system in a postoperative care setting based on pulse oximetry with nursing notification of violation of alarm setting via a wireless pager was associated with a 50–60% reduction for patient rescue and intensive care unit transfers. This certainly opens new possibilities in the improvement of patient care with devices that are well tolerated by the patient.

The effect of opioids on breathing depends on many interacting factors, including opioid potency, opioid speed of onset or offset, opioid receptor kinetics, dose and speed of infusion, route of administration, additional medication, site of surgery, surgical technique, underlying disease, age, sex, genetics, hormonal status (pregnancy), arousal, and pain (both of which are not constant in postoperative patients). Certainly, other factors may also play a crucial role (we could imagine that postoperative inflammatory and stress responses may play some role as well). We agree that improved understanding of opioid-induced effects on the control of breathing is required and argue that this is achieved by performing well-designed studies. Therefore, we encourage studies on the effect of opioids on the control of breathing; studies on “old” opioids, that is, opioids that are currently in use (see for example, Refs. 4 and 5), and on opioids under development, because at present we believe that it remains likely that an opioid that is devoid of respiratory depression is just not an opioid.

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