Respiratory Depression On The General Care Floor And Improved Monitoring: Are We Ready To Take The Next Step?

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Development and dissemination of this supplement has been possible with the support of Medtronic.
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Are We Ready To Take The Next Step?
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Introduction
In the last 30 years, we began creating awareness of the tragic harm suffered by patients who arrested on the ward, including retrospective evidence that warnings of deterioration in vital signs were missed or vital signs were simply not taken.¹,²,³ Published data from Get With the Guidelines® and other national resuscitation registries have repeatedly shown that unrecognized deterioration on the ward is not rare but common, and harm was often fatal, and not merely transient.³ Over the past fifteen years, clinician patient safety champions of ‘monitoring for all’ have worked with vendors to develop equipment that can answer the basic question for the frontline provider: “Is my patient in room 27 still breathing and have a pulse?”. The drawbacks of early solutions, including bulky equipment, alarm fatigue, tethered cables, capital acquisition cost, and other human factors and workflow deficiencies, have largely been solved. The technical advancements of ‘surveillance monitoring’ systems, defined as continuous electronic vital sign monitoring, have produced small, body borne, transducers without wires, low power requirements, distributed alarm notification, integrated EMR vital signs, and a use model that justifies their cost in terms of health and ‘human’ economics. Hospital systems that implemented surveillance monitoring now have enough data to share impressive and quantifiable improved clinical outcomes, and happier bedside clinicians.² It is time to communicate the vast improvements in the technology to our colleagues and administrators, push for nationwide adoption of surveillance monitoring guidelines, and urge patients and clinicians to demand continuous monitoring for all.

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Conflicts of Interest: All authors or their institutions report financial support to fund the Medtronic-sponsored PRODIGY trial. In addition, A. K. Khanna reports consulting fees from Medtronic, Edwards Lifesciences, and Philips North America. W. Buhre reports grants from the European Union and Interreg Consortium, and personal fees from European Society of Anaesthesiology studies (PHOENICS and TETHYS) supported by B Braun Medical and Fresenius Medical Care, and from Medtronic.
monitoring on the ward. Undetected and preventable clinical deterioration on the ward can then deservedly be put to rest.

**Risk of patient deterioration on the general care floor**

Approximately 150,000 cardiopulmonary arrests occur on the US ward every year, the vast majority of which are unwitnessed and the initial rhythm is nonshockable (asystole or PEA). Although the survival to discharge rate is improving due to rapid response teams and other factors, it remains low at 25%. Respiratory etiologies are the second most common cause of arrest, after cardiac causes, although cardiac etiology is often ‘checked’ as the default since there is no clear record of the decompensation time course. Surveillance monitoring is a key element in two of the three factors required to successfully identify patients decompensating or at risk for decompensation: education, monitoring and recognition. At risk patients can be identified by educated providers from the patients’ prior and active problem list and comorbidities, the treatments received (i.e. opioids, sedatives), and the trends and patterns of their vital signs. The physiologic signals and vital signs that are most commonly monitored by surveillance systems are hemodynamic and respiratory. Established evidence suggests patterns preceding decompensation are evident in respiratory rate; oxygen saturation; heart rate; blood pressure; and temperature. Most surveillance products provide all of this continuous data including blood pressure, with easy access to trends and patterns.

**Multi-parameter surveillance monitoring on the floor – combinations to improve patient safety**

The PRediction of Opioid-induced respiratory Depression In patients monitored by capnoGraphY (PRODIGY) study was an ambitious and comprehensive surveillance monitoring study, and has generated a wealth of continuous data on oxygen saturation, respiratory rate, etCO₂ and heart rate, (collected with a Capnostream™ 20p bedside monitor or Capnostream™ 35 portable respiratory monitor (Medtronic, Boulder, CO)) along with corresponding outcome data in both surgical and medical patients. A criticism of surveillance monitoring is that more data is not necessarily better data and will increase false alarms. Alarm fatigue has many causes but at its core is an outdated use of absolute threshold values to identify ‘abnormal’. PRODIGY and other continuous monitoring trials have shown that patterns of decompensation (duration, features, and severity), as originally described by Lynn and Curry for respiratory patterns, are evident and can differentiate a patient with a harmless transient desaturation below 90% from a patient who is in danger and likely to require rescue. This is evident from illustrations of real waveform data collected from PRODIGY.
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Figure 1 (A) showing cyclical desaturations and apneic pauses seen in a patient with obstructive sleep apnea and (B) monitoring detection of apneic episodes (blue dashed line) much before a clinical acute respiratory event (dark purple line) needing an emergent use of naloxone as a reversal agent. The cacophony of noise in our ICUs from threshold alarms will soon be replaced by alarms triggered by patterns of decompensation, derived from deep learning algorithms trained on monitoring data and incorporating a patient’s baseline values. Artificial intelligence systems already use deep learning to aide early recognition of sepsis in the ICU. Similarly, on the ward, surveillance monitoring data can support clinical recognition of decompensation without burdensome false alarms.

The PRODIGY trial makes an important contribution to the dataset needed to develop and implement these systems. It confirms that most of our care is safe, with few serious adverse events, but with clear evidence that in some instances, the patient’s physiologic rescue ability prevented critical decompensation, and we can do better to eliminate preventable, undetected decompensation.

**Using a risk prediction tool to help to determine a patient’s risk of respiratory depression**

Respiratory depression forms a clinically relevant risk factor during surgical patients’ recovery. PRODIGY was planned to determine a risk score for post-surgical and medical patients receiving parenteral opioids. A respiratory depression episode was defined as: respiratory rate $\leq 5$ bpm or oxygen saturation $\leq 85\%$, or end-tidal carbon dioxide $\leq 15$ or $\geq 60$ mmHg ($\geq 3$ minutes...
for any of these); apnea lasting >30 seconds; or any pre-specified respiratory Opioid-Related Adverse Event (ORADE).\textsuperscript{5} Initially, thresholds were based on expert opinion due the lack of available evidence. Continuous monitoring waveform data was evaluated by a group of independent experts to confirm true episodes versus artifact. The final data set showed that one or more continuous capnography and oximetry detected respiratory depression episodes occurred in 614 (46\%) of the 1,335 general care floor patients in the analyzed population.\textsuperscript{5} As a second step, a respiratory depression prediction model (adjusted AUC 0.74) was developed using five independent variables: age $\geq 60$ (in decades), male sex, opioid naïvety, sleep disordered breathing (defined as obstructive sleep apnea, the use of CPAP, or confirmation of the STOP questions in the STOP-BANG questionnaire), and chronic heart failure. Of these, age appeared to be the biggest driver of OIRD risk.\textsuperscript{5} Based on the maximum possible PRODIGY risk prediction score of 39 points, 3 risk groups were defined: high risk $\geq 15$, moderate risk $\geq 8$ and $<15$, and low risk $<8$ points.\textsuperscript{5} The PRODIGY score allowed effective risk discrimination between the high- and low-risk patient groups ($p<0.001$, OR 6.07, 95\% CI: 4.44-8.30).\textsuperscript{5} Therefore, clinicians can use the score to estimate the incremental risk of OIRD in ward patients. We strongly advocate external validation of the PRODIGY risk score in an independent cohort of medical and surgical patients.

**Personalizing monitoring to patient-specific need**

Modern day medicine demands that we continue to operate on patients with increased risks due to age, frailty and significant co-morbidities, where curative interventions are now more possible than ever before. In fact, the age demographic occupying inpatient beds across the world has shifted to a heavily geriatric population. While surgical and medical interventions for these patients continue to increase, patient monitoring on the ward has not kept pace. Due to a shortage of nurses and monitoring capabilities, only a small number of patients are effectively monitored in the general care setting. The most obvious underlying reasons are a shortage of monitoring devices and limited financial and personnel resources, but also a lack of knowledge about what patients will benefit the most from monitoring and early intervention to prevent a catastrophic event. We need to adopt the principles of precision medicine and individualized monitoring needs, providing a patient-tailored monitoring approach accounting for individual patient baseline clinical condition, type of procedure and adequate risk assessment. PRODIGY aims to evolve into an automated decision support tool allowing clinicians to use the right monitoring approach for individual patients. Any cardiorespiratory compromise episode may result in severe complications leading to cardiovascular collapse, and monitoring should focus on a personalized approach.
The cost of saving lives – economic implications of adding more surveillance monitoring on hospital wards

No monitoring is without cost constraints. However, respiratory depression events are expensive. In general, opioid related adverse drug events (ORADEs) are associated with a higher cost of hospitalization, ranging anywhere from 29% -47%.8,9 While ORADEs do not include respiratory depression only, specific cohorts, such as surgical patients that experience a respiratory ORADE, have reported a 10% increase in costs, or approximately $600 per patient.10 Other outcomes, such as increased readmission rates, longer lengths of hospital stay, and increased inpatient mortality add to the many layers of expenses associated with an avoidable event such as opioid-induced respiratory depression.8,9 Data from the PRODIGY trial supports these findings. Patients with respiratory depression had a longer average length of stay (10.5 ± 15.4 vs 7.7 ± 11.8 days; P < .0001) and US patients had higher hospital costs ($23,619 ± $16,868 vs $19,173 ± $13,549, p=0.0001) compared to patients without respiratory depression.5,11 A propensity weighted analysis identified 15% higher costs for US patients with respiratory depression (p=0.0013).11 Not surprisingly, length of stay significantly increased total cost. Transfers to higher levels of care (ICU) and the use of rapid response teams for rescue are very expensive. Other work has determined that continuous pulse oximetry and continuous capnography in patients receiving intravenous patient controlled analgesia opioids on the ward reduced rescue events and ICU transfers, and hence decreased healthcare costs.12,13 While the data seems compelling, a true cost effectiveness analysis is needed to compare the cost of using continuous monitoring versus the cost of these specific events on a dollar to dollar basis. In addition, experiments should be designed to specifically compare traditional spot-check versus continuous monitoring and estimate the cost of missed hypoxemia and hypoventilation either alone or in combination.

Monitoring in the COVID-19 era

The SARS-CoV-2 pandemic presents unique challenges to healthcare and patient safety. Typical presentation includes fever and cough with radiographic evidence of pneumonia and shortness of breath.14 However, not all of these patients need hospitalization, and even for those who do, a large proportion do not meet criteria for admission to critical care. Furthermore, critical care beds are an expensive and valuable resource, and the triage decision to leave COVID-19 patients on a relatively under-monitored floor environment or non-monitored home care is one that is tricky at best. This means patients who stay home and self-monitor symptoms are essentially relying on surveillance of themselves and their own vital signs. Those on the ward are being monitored, at best, every 4-6 hours. Knowing that up to 90% of all hypoxemia episodes lasting up to an hour
are missed with spot-check monitoring, we risk missing one of the most basic signs of patient deterioration with COVID-19.\textsuperscript{15} This is important since some COVID-19 pneumonia has uniquely presented with ‘happy hypoxia’ wherein patients can desaturate to the 50s to 70s and do not appear to have increased work of breathing or subjective symptoms of respiratory distress.\textsuperscript{16} These patients are at great risk of sudden decline and this may be why so many deceased COVID-19 patients never made it to the hospital. Continuous oximetry may serve an important unmet need for our patients and help with important decision making. Early prediction of respiratory failure is also critical since delaying endotracheal intubation may be associated with swings in transpulmonary pressures, vascular flows and fluid leakage, all potential contributors to COVID-19 lung injury.\textsuperscript{17} An attractive monitoring technique for early deterioration is the pulse oximetry waveform, which is a depiction of the arterial pulse and is affected by variations in respiratory pressures due to the phenomenon of pulsus paradoxus. Physiological parameters that reflect respiratory-induced changes in the pulse oximetry plethysmographic (POP) waveform can reflect these changes.\textsuperscript{18} Herein, a simple extension of this application implemented in a continuous monitoring tool will help predict impending respiratory failure and the need for intubation in COVID-19 patients.\textsuperscript{19} Monitoring remains critical in the era of the pandemic, and will need to be portable, reliable, preferably touchless, and built with an effective alert and response system.

**Conclusions**

Patients recovering in non-critical areas are a vulnerable population that continue to experience cardiorespiratory compromise, some of which may be sudden and catastrophic. These events are usually preceded by several hours of a gradual pattern change of vital signs that may not be detected using traditional intermittent spot-check monitoring. The risk of monitoring everyone at all times must be balanced with the risk of false alarms and resultant fatigue. The PRODIGY risk score is an easy to use bedside tool that accurately predicts the risk of respiratory depression episodes in patients receiving parenteral opioids. This will allow effective risk stratification of ward patients who may benefit from continuous monitoring and concomitant early intervention to prevent critical events.

**References**


