EM Advances

A comparative evaluation of capnometry versus pulse oximetry during procedural sedation and analgesia on room air

Marco L.A. Sivilotti, MD, MSc;*† David W. Messenger, MD;* Janet van Vlymen, MD;† Paul E. Dungey, MD;* Heather E. Murray, MD, MSc*§

ABSTRACT

Objective: Important questions remain regarding how best to monitor patients during procedural sedation and analgesia (PSA). Capnometry can detect hypoventilation and apnea, yet it is rarely used in emergency patients. Even the routine practice of performing preoxygenation in low-risk patients is controversial, as supplementary oxygen can delay the detection of respiratory depression by pulse oximetry. The purpose of this study was to determine whether the capnometer or the pulse oximeter would first detect respiratory events in adults breathing

Methods: During a randomized clinical trial comparing fentanyl with low-dose ketamine for PSA with titrated propofol, patients were monitored using pulse oximetry and continuous oral–nasal sampled capnography. Supplemental oxygen was administered only for oxygen desaturation. Sedating physicians identified prespecified respiratory events, including hypoventilation (end-tidal carbon dioxide > 50 mm Hg, rise of 10 mm Hg from baseline or loss of waveform) and oxygen desaturation (pulse oximetry < 92%). These events and their timing were corroborated by memory data retrieved from the monitors.

Results: Of 63 patients enrolled, 57% (36) developed brief oxygen desaturation at some point during the sedation. All responded to oxygen, stimulation or interruption of propofol. Measurements of end-tidal carbon dioxide varied substantially between and within patients before study intervention. Hypoventilation (19 patients, 30%) was only weakly associated with oxygen desaturation (crude odds ratio 1.4 [95% confidence interval 0.47 to 4.3]), and preceded oxygen desaturation in none of the 12 patients in whom both events occurred (median lag 1:50 m:ss [interquartile range 0:01 to 3:24 m:ss]).

Conclusion: During PSA in adults breathing room air, desatu-

ration detectable by pulse oximeter usually occurs before overt changes in capnometry are identified.

Keywords: conscious sedation, procedural sedation, capnography, oximetry, propofol, respiratory depression

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RÉSUMÉ

Objectif: Des questions importantes demeurent quant à la meilleure méthode de monitorage des patients pendant la sédation et l'analgésie procédurales (SAP). La capnométrie permet de détecter une hypoventilation et l'apnée, mais elle est rarement utilisée à l'urgence. Même la préoxygénation en pratique de routine chez les patients à faible risque est controversée, l'oxygène supplémentaire pouvant retarder la détection d'une dépression respiratoire par oxymétrie de pouls. Le but de cette étude était de déterminer si la capnométrie ou l'oxymétrie de pouls détecteraient précocément les événements respiratoires chez les adultes respirant l'air ambiant.

Méthodes: Au cours d'un essai clinique randomisé comparant l'administration de fentanyl à celle de kétamine à faible dose pour la SAP par le propofol à posologie ajustée, les patients ont été surveillés à l'aide de l'oxymétrie de pouls et par le prélèvement continu d'échantillons buccaux/nasaux par capnographie. L'oxygène d'appoint a été administré uniquement pour la désaturation en oxygène. Les médecins administrant les agents sédatifs ont détecté des événements respiratoires prédéterminés, y compris l'hypoventilation (dioxyde de carbone en fin d'expiration > 50 mm Hg, une hausse de 10 mm Hg par rapport à la base de référence ou perte de tracé capnographique) et une désaturation en oxygène (oxymétrie de pouls < 92 %). Ces événements et le moment de leur survenue ont été corroborés par des

From the Departments of *Emergency Medicine, †Pharmacology & Toxicology, ‡Anesthesiology and §Community Health & Epidemiology, Queen's University, Kingston, Ont.

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données-mémoire extraites des moniteurs.

Résultats: Parmi les 63 patients qui ont participé à l'étude, on a noté une brève désaturation en oxygène chez 57 % (36) à un moment donné pendant la sédation. Ils ont tous répondu à l'apport d'oxygène, à la stimulation ou à l'interruption de propofol. La mesure du dioxyde de carbone en fin d'expiration variait considérablement entre les patients et chez les patients mêmes avant l'intervention de l'étude. L'hypoventilation (19 patients, 30 %) n'a été que légèrement associée à une désatura-

tion en oxygène (ratio d'incidence approché brut de 1,4 [intervalle de confiance à 95 %, de 0,47 à 4,3]), et ne précédait la désaturation en oxygène chez aucun des 12 patients chez lesquels les deux événements se sont produits (retard médian de 1:50 m:ss [intervalle interquartile de 0:01 à 3:24 m:ss]).

Conclusion: Au cours de la SAP chez les adultes respirant l'air ambiant, la désaturation détectable par oxymétrie de pouls survient habituellement avant que des changements manifestes en capnométrie soient détectés.

INTRODUCTION

During the last decade, emergency physicians have embraced procedural sedation and analgesia (PSA) and made it a routine component of care. Nevertheless, important safety questions remain regarding the type of monitoring to use during and after sedation. Specifically, the role of capnometry, which can detect hypoventilation or apnea by measuring exhaled carbon dioxide, and the merits of routine preoxygenation in low-risk patients remain controversial in the emergency department (ED) setting.¹⁻¹⁰

Capnography, which displays a continuous exhaled carbon dioxide waveform, has been the standard of care in the operating room for patients receiving mechanical ventilation for nearly 2 decades, in part to signal interruption of the ventilator circuit.¹¹ Emergency physicians recognize that detection of exhaled carbon dioxide is the preferred method to confirm placement of the endotracheal tube following intubation. In patients not receiving mechanical ventilation, capnometry can be used to estimate ventilation and airway patency.6 However, emergency medicine specialty societies have not endorsed its routine use for PSA.7,10 Some researchers have used capnometry to detect "subclinical respiratory depression" during PSA, 2,5,9,12-19 but the ability of this technology to identify clinically important end points remains unclear. In fact, few Canadian EDs have ready access to capnography, or use any form of respiratory monitoring during PSA apart from pulse oximetry.^{6,20}

During the course of a randomized controlled trial of ketamine–propofol versus fentanyl–propofol for ED PSA in adults breathing room air, continuous capnometry was used for monitoring of patients.²¹ As a secondary study question, we hypothesized that this additional monitoring could improve patient safety by detecting respiratory depression earlier. The purpose of this study was to determine which monitor would first detect a respiratory event: the pulse oximeter or the capnometer.

METHODS

Study design and setting

We performed a planned, secondary analysis nested within a randomized, double-blind clinical trial, which compared low-dose ketamine to fentanyl for PSA using titrated propofol. The trial took place in the ED of a university-affiliated tertiary care hospital between December 2004 and February 2006 and is described in detail elsewhere.²¹ The study was approved by the institutional ethics board, and all participants provided written informed consent.

Study population

We enrolled American Society of Anesthesiology Physical Status Class I or II patients aged 14 to 65 years undergoing PSA for orthopedic reduction or abscess drainage. Seven emergency physicians (4 senior residents, 3 attending physicians) trained in study procedures were available on-call to enrol participants and perform study sedations. We excluded patients with significant active cardiac, pulmonary, hepatic or renal disease, recent substance abuse or prior opioid dependence, obstructive sleep apnea, prior psychosis, or allergy or sensitivity to ketamine, fentanyl or propofol. We also excluded patients who weighed more than 130 kg, were opioid users or were acutely intoxicated.

Study procedure and equipment

Participants were monitored using a LifePak 12 with capnography (Medtronic ERS), which displays a continuously sampled carbon dioxide waveform as well as the most recent end-tidal carbon dioxide value. The manufacturer reports an accuracy of \pm 4 mm Hg for readings below 38 mm Hg and \pm 12% for readings between 39 and 99 mm Hg. Continuous pulse oximetry, electrocardiography and noninvasive blood pressure were also displayed

on the same monitor. All participants wore the manufacturer-recommended cannula (Nellcor Smart Capnoline O₂/CO₂ Oral Nasal Cannula, Tyco Healthcare) to allow continuous oral–nasal sidestream carbon dioxide sampling at 50 mL/min. By protocol, the cannula was connected to a closed oxygen source at baseline. Supplemental oxygen was administered only if patients developed oxygen desaturation, in keeping with our usual practice for otherwise healthy adults and consistent with national guidelines¹⁰ and local policy. One nurse and at least 2 physicians were present throughout the procedure.

Participants were randomly assigned to groups receiving either 0.3 mg/kg ketamine or 1.5 µg/kg fentanyl intravenously as the study intervention at time zero. Two minutes later, all patients were given 0.4 mg/kg propofol intravenously, followed by additional 0.1 mg/kg boluses every 30 seconds as required to achieve and maintain a score of 1 on the Modified Observer's Assessment of Alertness/Sedation Scale (i.e., responding only to painful stimuli).²² Prespecified thresholds for airway, respiratory and hemodynamic interventions were established by protocol. Sedating physicians were allowed to initiate any supportive measure at their discretion.

Definitions of outcomes

Using the thresholds most commonly cited in the literature and by consensus among the investigators, we originally defined hypoventilation to be an absolute end-tidal carbon dioxide greater than 50 mm Hg at any point, a relative rise of greater than 10 mm Hg from presedation baseline, a loss of waveform on the capnograph for longer than 30 seconds or recurrent losses of waveform for briefer periods. 9,12,13,16,17,19,23,24 Because others have proposed using a decrease of 10 mm Hg from baseline as a measure of abnormal ventilation, 5,9,13,15 we added this criterion to our definition and designated the expanded outcome abnormal capnometry. Oxygen desaturation was defined as pulse oximetry less than 92%. Unless otherwise specified, timed end-tidal carbon dioxide and pulse oximetry readings recorded in monitor memory were used for all analyses, including the determination of a baseline value before administration of the study drug.

Data collection and analysis

Sedating physicians entered data prospectively onto a standardized data form. Prespecified cardinal events including oxygen desaturation and hypoventilation were listed on this form. These events served as thresholds for specific interventions by the sedating physician, as detailed on the form and as explained to study physicians during their training session. Sedating physicians were instructed to push the "Event" button on the monitor at time zero and during cardinal events. The monitor was set by the manufacturer to alarm after 30 seconds of no exhaled carbon dioxide reading over 8 mm Hg, or if pulse oximetry fell below 90%. The monitor recorded into memory a complete set of vital signs including end-tidal carbon dioxide every 3 minutes, whenever the "Event" button was pressed, and whenever a monitor alarm threshold was reached. After patient recovery, the entire record of the sedation including all timed vital signs were printed to paper using the "Code Summary" function, and compared with the baseline vitals, events and timing recorded by the sedating physician on the study form.

There was no a priori null hypothesis tested, and descriptive statistics alone are presented.

RESULTS

We enrolled a total of 63 patients who underwent PSA, the majority for reduction of a fracture or a dislocation. The mean age of participants was 39 (standard deviation [SD] 18) years and 51% (SD 32%) were women (Table 1). The primary trial was stopped by the data monitoring committee following a planned interim

Table 1. Characteristics of 63 participants who underwent procedural sedation and analgesia with ketamine or fentanyl

	Mean (SD)*		
Characteristic	Ketamine, n = 32	Fentanyl, $n = 31$	
Age, yr	36 (17)	43 (7)	
Female sex, no. (%)	12 (38)	20 (65)	
Weight, kg	75 (16)	77 (5)	
Type of procedure, no. (%)			
Orthopedic	31 (97)	27 (87)	
Abscess drainage	1 (3)	4 (13)	
Pain score before the procedure, out of 10	4.6 (2.4)	5.9 (2.5)	
Baseline vital signs			
Heart rate, beats/min	88 (15)	83 (17)	
Systolic blood pressure, mm Hg	142 (18)	138 (19)	
Diastolic blood pressure, mm Hg	84 (11)	84 (14)	
Aterial pressure, mm Hg	105 (12)	103 (15)	
Oxygen saturation, %	98.4 (1.5)	97.6 (2.7)	
End-tidal carbon dioxide, mm Hg	39.4 (5.8)	38.7 (4.7)	

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analysis at 50% enrolment when an important difference in safety emerged in favour of ketamine.²¹ This effect was primarily driven by oxygen desaturation, which was particularly frequent in the fentanyl group. Overall, more than half of the participants developed oxygen desaturation below 92% at some point (Table 2). In all cases, the oxygen desaturation was brief and uncomplicated, and responded immediately to supplemental oxygen, interruption of propofol administration or stimulation of the patient.

Values of end-tidal carbon dioxide before administration of the study drug fluctuated widely between and within participants. The baseline value closest to time zero, as retrieved from the monitor memory, varied substantially among participants (mean [SD] 39.3 [4.9] mm Hg [95% confidence interval (CI) 29.5 to 49.1 mm Hg]) (Fig. 1). The presedation end-tidal carbon dioxide value as recorded by the study physician on the study form differed by up to 5 mm Hg from the monitor memory

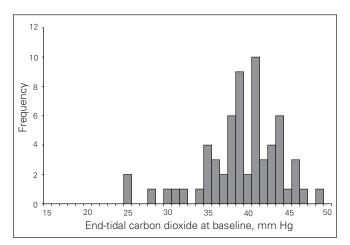


Fig. 1. Measurements of end-tidal carbon dioxide before study interventions.

value (difference 0.1 [SD 2.7] mm Hg [95% CI –5.2 to 5.5 mm Hg]; range –6 to 7 mm Hg). In addition, there was considerable variation within participants in the absence of any intervention. Readings of serial endtidal carbon dioxide recorded in monitor memory for any given participant fluctuated by about 5 mm Hg in either direction in the few minutes before drug administration (Fig. 2). In contrast, pulse oximetry values were highly consistent at baseline (median 99% [95% CI 94% to 100%]).

In total, 19 patients (30%) met the prespecified criterion for hypoventilation, usually as a result of loss of capnograph waveform, independent of study group assignment (Table 2). The apnea alarm was triggered in 3 of these cases by a loss of waveform. In 5 cases, 4 of which

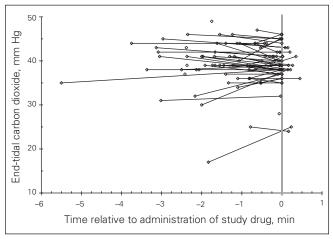


Fig. 2. Individual end-tidal carbon dioxide measurements just before study intervention (patient at rest). Lines join measurements obtained from the same patient as retrieved from monitor memory. The difference between the 2 end-tidal carbon dioxide measurements in each patient just before administration of the study drug is (mean [standard deviation]) 0.0 (2.5) mm Hg (95% confidence interval –5.0 to 5.1 mm Hg).

Table 2. Incidence of prespecified respiratory events, overall and by study group					
Respiratory event	No. (%) of patients				
	Overall, $n = 63$	Ketamine, $n = 32$	Fentanyl, $n = 31$	Difference (95% CI)	
Oxygen desaturation	36 (57)	_	_	_	
Oxygen saturation < 92% at any time	36 (57)	12 (38)	24 (77)	-40 (-62 to -8)	
Oxygen saturation < 80% at any time	13 (21)	1 (3)	12 (39)	-36 (-54 to -17)	
Oxygen saturation < 70% at any time	4 (6)	0 (0)	4 (13)	-13 (-25 to -1)	
Hypoventilation	19 (30)				
Rise in end-tidal carbon dioxide > 10 mm Hg above baseline	7 (11)	3 (9)	4 (13)	-4 (-19 to12)	
End-tidal carbon dioxide > 50 mm Hg	6 (10)	1 (3)	5 (16)	-13 (-30 to 3)	
Loss of end-tidal carbon dioxide waveform for > 30 s or recurrent loss	12 (19)	5 (16)	7 (23)	-7 (-26 to 12)	
CI = confidence interval.					

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were due to a relative rise of 10 mm Hg in end-tidal carbon dioxide, the hypoventilation was detected only on retrospective review of the monitor data, as the sedating physician failed to identify the abnormal capnometry.

The association between oxygen desaturation and hypoventilation was weak (crude odds ratio 1.4 [95% CI 0.47 to 4.3]). Hypoventilation never preceded oxygen desaturation in the 12 patients in whom both events occurred. On average, oxygen desaturation was identified nearly 2 minutes before changes in capnometry (median 1:50 min:s [interquartile range 0:01 to 3:24 min:s], range 0:00 to 12:09 min:s). Moreover, the remaining 67% of patients (24/36) with oxygen desaturation never met the a priori definition for hypoventilation.

In some participants, end-tidal carbon dioxide *fell* during sedation. A total of 30 patients (48%) demonstrated abnormal capnometry. The strength of association between oxygen desaturation and abnormal capnometry was slightly stronger (crude odds ratio 2.8 [95% CI 0.99 to 7.9]). However, 42% (15/36) of patients with oxygen desaturation never met even this broader definition. In only 2 of the remaining 21 cases did the abnormal capnometry precede oxygen desaturation (median time difference between oxygen desaturation and abnormal capnometry 2:04 min:s [interquartile range 0:01 to 5:55 min:s], range –2:57 to 12:09 min:s) (Fig. 3).

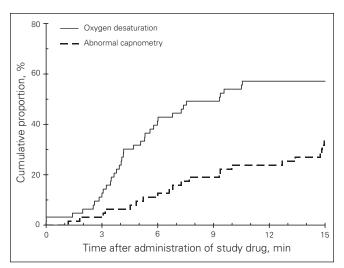


Fig. 3. Relative time to oxygen desaturation, hypoventilation or fall in end-tidal carbon dioxide. The time to oxygen desaturation (oxygen saturation < 92% at any time) for all participants is shown as a solid line. Among those patients who developed desaturation, the time to abnormal capnometry (end-tidal carbon dioxide > 50 mm Hg, a rise > 10 mm Hg over baseline or a loss of waveform) is represented by the dashed line. Capnometric abnormalities were observed in only half of those patients who experienced oxygen desaturation and generally occurred several minutes later.

DISCUSSION

During this prospective study nested within a clinical trial, we observed several difficulties with using capnometry to monitor adult patients undergoing PSA in the ED. First, substantial variability among and within participants in capnometry before study interventions made it difficult for physicians to establish a reliable baseline value against which to measure changes. Second, study physicians often failed to recognize a 10 mm Hg rise in end-tidal carbon dioxide during the sedation, likely due in part to the aforementioned baseline variability. Third, and most importantly, capnometric abnormalities were poorly sensitive and late findings in patients with respiratory depression as manifested by oxygen desaturation on room air. As such, in patients who did not receive preoxygenation, capnometry did not offer any apparent benefit over pulse oximetry for the detection of respiratory depression.

A fall in end-tidal carbon dioxide of 10 mm Hg may occasionally precede subsequent oxygen desaturation. Although it is counterintuitive to use a decrease in end-tidal carbon dioxide as a marker of hypoventilation, this decrease may be caused by changes in spontaneous breathing, such as more shallow breaths, partial breath holding or intermittent partial airway obstruction. Hypoventilation with diminished tidal volume breaths results in increased dead-space fraction and decreased end-tidal carbon dioxide, a pattern termed hypopneic hypoventilation. It is doubtful, however, that a decrease in end-tidal carbon dioxide is more likely to be recognized by a sedating physician than an increase, or that a more complex definition of abnormal capnometry will improve the utility of this instrument.

Capnography is the standard of care for patients receiving mechanical ventilation support in the operating room, and is the preferred method to confirm endotracheal tube placement. Advocates of capnography for patients not receiving mechanical ventilation propose that capnography is the best measure of ventilation, which does not necessarily correlate with oxygenation, especially in patients on supplemental oxygen. But, as with any device, the benefits of capnography need to be quantified in the target population before its routine incorporation into clinical practice.

The Canadian Association of Emergency Physicians consensus guidelines on PSA do not discuss capnography, but note that "oxygen administration may increase oxygen saturation in the face of hypoventilation, and ... undetected CO₂ retention may occur." The more recent

American College of Emergency Physicians clinical policy suggests capnography be considered at a level C recommendation, as it may "detect early cases of inadequate ventilation before oxygen desaturation takes place."7 This clinical policy also states that "the administration of oxygen ... may delay ... the detection of hypoventilation." The consensus uniform reporting standards recently proposed by 2 large pediatric emergency research consortia for PSA in children mention capnography only in passing, and do not specify clinically important changes in capnometry.31,32 Guidelines of The Canadian Anesthesiologists' Society state that capnography is required only when an endotracheal tube or laryngeal mask airway is being used.11 The consultants who developed the American Society of Anesthesiologists Practice Guidelines for Sedation and Analgesia by Non-anesthesiologists could not agree whether capnography decreased risks during moderate sedation, but did conclude "that it may decrease risks during deep sedation."2,5,33

Only a few published emergency medicine studies are relevant to this issue, and all had relatively small sizes, especially for a safety outcome. 1,2,5,9,12–19,34 These studies are also difficult to summarize because of widely variable patient ages, sedating practices and definitions of abnormal capnometry. Many of the patients in these studies were administered supplemental oxygen before sedation. Finally, the clinically relevant issue of which monitor is the first to detect an abnormality has only been explicitly addressed in 3 prior studies, one of which involved children and the other 2 adults administered supplemental oxygen. 15,34

The wide range among patients of end-tidal carbon dioxide values at baseline before any intervention has been previously noted, 9,12,25,35 as has the existence of considerable breath-to-breath variability.6 Without a consistent baseline value, the clinical significance of relative changes of only 10 mm Hg in either direction becomes unclear. It is even more difficult to accept using a 10% change from baseline as being abnormal, as has recently been proposed.^{2,34} Such changes are typically smaller than the accuracy of the instrument itself. A relative change of 10% was observed in 6 of our participants at baseline in the few minutes before any study intervention. Although recording and analyzing these changes for research purposes may be worthwhile, clinicians require a more easily interpreted, real-time information stream similar to what is provided by pulse oximetry.

Pulse oximetry was rapidly accepted to be the standard of care and is widely used largely because its benefits are self-evident, the need for interpretation and training minimal, it is robust under a variety of suboptimal clinical circumstances, and it allows for the immediate and reliable identification of hypoxemia. The same properties do not appear to hold for capnometry, a distinct and complementary monitoring technology which evaluates ventilation rather than oxygenation.

Our findings support the conclusion that pulse oximetry allows earlier detection of respiratory depression when patients breathe room air, especially during the critical initial phase of medication titration to an appropriate plane of sedation. 9,36-40 Pulse oximetry appears to have many advantages over capnometry to detect a lower safety threshold and limit overshoot medication dosing. Earlier recognition of the important end point of excessive propofol in our study allowed rapid correction, and served as a natural signal to the sedating physician. This conclusion is supported by recent data from a simulator laboratory.⁴

Although more information is generally regarded as being better for patient safety, redundant information, falsely reassuring information, false alarms and information overload can both distract and mislead clinicians. These concerns are particularly an issue during the initial phase of PSA when the physician must simultaneously analyze multiple information sources to reach the proper level of sedation and analgesia. Inattention becomes a greater concern during the much longer periods commonly encountered in the operating room environment. Experts concede that "capnographic abnormalities are commonly transient and of no clinical consequence." 22

Strengths and limitations

The strengths of this study flow from its design, nested within a prospective clinical trial, which allowed diligent data collection, prespecified definitions, a homogenous patient sample, consistent drug titration, a small number of trained study physicians performing sedations and collecting data, and independent corroboration of physician observations with the monitor's automatic alarms and timed data in memory.

The study's main limitation is that enrolled participants were relatively healthy adults breathing room air. These findings cannot be extrapolated to other populations. In fact, we would expect that capnometry has an important role in detecting more advanced respiratory depression masked by the use of supplemental oxygen. Many emergency physicians routinely perform preoxygenation in low-risk patients before PSA.³ We cannot

exclude the possibility that the capnograph provided relevant information once supplemental oxygen was administered to those participants who developed desaturation more than a few minutes before the end of the procedure. Furthermore, it is recognized that experts can identify subtle findings of nonturbulent partial airway obstruction, bronchospasm, pulmonary embolus and other pathologic conditions in the capnograph waveform.^{25,28} Our findings are not intended to devalue these benefits of capnography, especially in patients receiving mechanical ventilation, or for research purposes. Indeed, the shape of the waveform is likely more informative than the actual end-tidal carbon dioxide reading.^{6,25,35} Finally, the software limitations of our monitor did not allow capture and independent analysis of the waveform itself, nor did we reprogram the monitor threshold to alarm at 92% oxygen saturation.

CONCLUSION

During PSA in adults breathing room air, desaturation detectable by pulse oximeter usually occurs before overt changes in capnometry are identified. Moreover, substantial variation among and within participants in end-tidal carbon dioxide values at baseline hampers the identification of clinically important changes in capnometry. These findings should not be extrapolated to patients administered supplemental oxygen where it is possible capnometry may be helpful. Future research should focus on developing more consistent and clinically applicable definitions of abnormal exhaled carbon dioxide values and waveforms, to help determine whether this technology provides a convincing safety benefit over current practice.

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Correspondence to: Dr. Marco Sivilotti, 76 Stuart St., Department of Emergency Medicine, Queen's University, Kingston ON K7L 2V7; marco.sivilotti@queensu.ca

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