When Seconds Count, Buy More Time

The Oxygen Reserve Index and Its Promising Role in Patient Monitoring and Safety

Allan F. Simpao, M.D., M.B.I., Jorge A. Gálvez, M.D.

THE pulse oximeter has become a virtually indispensable monitor for measuring a patient's peripheral capillary oxygen saturation (Spo_2) accurately and reliably in a continuous, noninvasive fashion.[1] Despite its ubiquitous use as a detector of hypoxemia, pulse oximetry has limited utility to herald an oxygen desaturation event until the partial pressure of oxygen (Pao_2) falls below 80 mmHg. Above this threshold, a patient's Spo_2 will typically remain at or near 100%, whereas Pao_2 drops; by the time the Spo_2 falls, the patient's Pao_2 may be accelerating quickly past the inflection point of the oxygen–hemoglobin dissociation curve and proceed to decrease rapidly.[2] In this issue of Anesthesiology, Szmuk *et al.*[3] present a pilot study of the oxygen reserve index (ORI), a novel pulse oximeter–based nondimensional index that may provide a clinically important warning of impending desaturation in patients who have increased Pao_2 levels. The authors report results from a prospective clinical trial in children that measured ORI after preoxygenation, induction of general anesthesia, successful tracheal intubation, and then disconnection of the anesthesia circuit. Their major finding was that the ORI indicated impending desaturation at a median of 31.5 s (interquartile range, 19 to 34.3 s) before noticeable changes in Spo_2 occurred.

"Every second counts during those crucial moments, and novel technology that has the potential to warn clinicians sooner than the current technology is worth a much closer look."

The authors performed a prospective cohort study at a single, tertiary pediatric hospital. A total of 25 healthy children aged 3 to 12 yr were studied using a pulse oximeter that was equipped to collect the optical raw data needed to compute ORI. Anesthesia was induced with 8% sevoflurane in 100% O_2 supplemented by intravenous propofol and fentanyl. On confirmation of tracheal intubation, the anesthesia circuit was disconnected to eliminate apneic oxygenation, and the saturation was permitted to fall to 90%. The anesthesia circuit was reconnected immediately, and the patients were ventilated with 100% oxygen. The ORI and Spo_2 values were recorded at 1-s intervals at the beginning of apnea, beginning and end of intubation, beginning and end of the ORI alarm (calculated offline using the manufacturer's proprietary algorithm), and 2 min after reoxygenation. The authors defined the early warning time as from the beginning of the rapid decrease of the ORI values (indicated by the start of the reserve index alarm), until saturation reached 98%. Alarm activation was based on the rate of change in ORI not on a specific ORI value. The ORI was at 0 (its minimum value) when Spo_2 was less than 98% and increased rapidly as Spo_2 increased to 99% and higher during reoxygenation.

The authors' study of ORI bears significant promising clinical and translational implications. The traditional process of intubation *via* direct laryngoscopy and tracheal tube placement in preoxygenated, apneic patients involves some guesswork. Clinicians must constantly estimate a patient's oxygen reserve and how much time remains to intubate safely before the attempt must be aborted and ventilation must be resumed. Although pulse oximetry can help to prevent anesthesia-related mishaps during this process, the monitor's lag time makes it a suboptimal detector of impending hypoxemia.[4,5] Indeed, despite the widespread availability and use of pulse oximetry and capnography, the most common acute severe complications in pediatric anesthesia are related to airway management and the respiratory system.[6] ORI has the potential to answer one of the most crucial questions during intubation: how

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Corresponding article on page 779.

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much time does the patient have remaining for this intubation attempt before he or she desaturates? As Szmuk *et al.* have shown, ORI takes a ubiquitous early warning system and makes it an even *earlier* warning system. In addition, ORI can indicate when patients have been adequately preoxygenated and might have utility as an adjunct monitor of hypoventilation in patients who are on supplemental oxygen and whose Pa_{O_2} is increased.

The study design was appropriate for a pilot study, and the study subjects and anesthetic protocol reflect typical pediatric anesthesia practice. The monitor used for this study was not equipped to display ORI; thus, investigators were blinded to the ORI values throughout the study period. Measurements were made with adequate granularity (1-s intervals). However, the study had several weaknesses and limitations, many of which the authors mention: the authors did not test the utility of ORI in abnormally high oxygen consumption states; the study population was small in number and consisted entirely of preoxygenated, apneic healthy children; no arterial blood gas sampling was performed to determine the correlation between ORI and Pa_{O_2}; the ORI measurements were obtained from a pulse oximetry sensor on the patient's toe, which likely increased the Sp_{O_2} delay in the setting of acute hypoxemia[7]; and ORI was validated in a study of 11 adult volunteers that was neither peer reviewed nor published. Finally, ORI remains available only for investigational use in the United States.

Pulse oximetry is used worldwide every day despite minimal empirical evidence that the monitor improves outcomes,[8] although some have argued that at this point pursuing such research would be similar to designing a randomized controlled trial to prove that parachutes are safe.[9] Szmuk *et al.* have provided an exciting pilot study of a promising advancement in pulse oximetry technology. This study is an important first step in understanding the clinical utility and relevance of ORI and how it can improve patient monitoring and safety in the perioperative setting and throughout the hospital. Substantial work remains to determine the accuracy and reliability of ORI and to validate and optimize the ORI alerts in various patient populations—particularly in higher risk patients such as children, parturients, the critically ill, and those with diminished pulmonary reserve. All anesthesiologists should appreciate advanced warning of impending oxygen desaturation. Every second counts during those crucial moments, and novel technology that has the potential to warn clinicians sooner than the current technology is worth a much closer look.

Competing Interests

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Oxygen Reserve Index

A Novel Noninvasive Measure of Oxygen Reserve—A Pilot Study

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ABSTRACT

Background: Pulse oximetry provides no indication of downward trends in Pa_{O_2} until saturation begins to decrease. The Oxygen Reserve Index (ORI) is a novel pulse oximeter–based nondimensional index that ranges from 1 to 0 as Pa_{O_2} decreases from about 200 to 80 mmHg and is measured by optically detecting changes in Sv_{O_2} after Sa_{O_2} saturates to the maximum. The authors tested the hypothesis that the ORI provides a clinically important warning of impending desaturation in pediatric patients during induction of anesthesia.

Methods: After preoxygenation, anesthesia induction, and tracheal intubation, the anesthesia circuit was disconnected and oxygen saturation was allowed to decrease to 90% before ventilation recommenced. The ORI and Sp_{O_2} values were recorded from a Masimo Pulse Co-Oximeter Sensor at the beginning of apnea, beginning and end of intubation, beginning and end of the ORI alarm, and 2 min after reoxygenation.

Results: Data from 25 healthy children, aged 7.6 ± 4.6 yr, were included in the analysis. During apnea, the ORI slowly and progressively decreased over a mean of 5.9 ± 3.1 min from 0.73 ± 0.16 at the beginning of apnea to 0.37 ± 0.11. Sp_{O_2} remained 100% throughout this initial period. Concurrently with alarm activation, the ORI began to decrease rapidly, and in median of 31.5 s (interquartile range, 19 to 34.3 s), saturation decreased to 98%.

Conclusions: In this pilot study, the ORI detected impending desaturation in median of 31.5 s (interquartile range, 19–34.3 s) before noticeable changes in Sp_{O_2} occurred. This represents a clinically important warning time, which might give clinicians time for corrective actions. **(Anesthesiology 2016; 124:779-84)**

THE relationship between the arterial oxygen saturation (Sa_{O_2}) and the partial pressure of oxygen (Pa_{O_2}) is characterized by the oxyhemoglobin dissociation curve that incorporates three distinct ranges: hypoxia, normoxia, and hyperoxia. The relationship follows a well-described sigmoidal curve until Pa_{O_2} reaches about 80 mmHg or greater and the corresponding Sa_{O_2} remains nearly constant at 100%. But at higher oxygen partial pressures, Sa_{O_2} cannot increase further. Thus, pulse oximetry (Sp_{O_2}) cannot assess oxygen partial pressure once hemoglobin is fully saturated. That the relationship between oxygen partial pressure and hemoglobin saturation plateaus when Pa_{O_2} exceeds about 80 mmHg is generally of little consequence because anesthesiologists are most concerned about low partial pressures of oxygen and rather less so about the large range of partial pressures that fully saturate hemoglobin.

However, there are situations in which it is helpful to know the partial pressure of oxygen in full saturated blood.

What We Already Know about This Topic

- Oxygen supplementation delays detection of hypoventilation by pulse oximetry in both adults and children because oxyhemoglobin saturation remains 100% over a wide range of oxygen partial pressures exceeding about 80 mmHg
- The Oxygen Reserve Index is a nondimensional index that ranges from 1 (much reserve) to 0 (no reserve) and is measured by optically detecting changes in Sv_{O_2} after Sa_{O_2} saturates to the maximum
- The goal of this pilot study was to test the hypothesis that the Oxygen Reserve Index provides a clinically important warning of impending desaturation in pediatric patients during induction of anesthesia

What This Article Tells Us That Is New

- During prolonged apnea in healthy anesthetized children, the Oxygen Reserve Index detected impending desaturation in median of 31.5 s (interquartile range, 19 to 34.3 s) before noticeable changes in Sp_{O_2} occurred

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For example, very high partial pressures of oxygen—even for minutes—promote atelectasis[1]; and over days, high partial pressures cause pulmonary injury in critical care patients[2] and retinal injury in premature infants.[3] But there is also a common situation in which having an estimate of oxygen partial pressure of fully saturated blood would be clinically useful: during induction of anesthesia. Most patients are given 80 to 100% oxygen for several minutes before induction of anesthesia. The primary reason is that filling the functional residual capacity of the lungs provides several minutes worth of oxygen "reserve" in case of airway compromise.

Once desaturation starts during an airway crisis, it typically progresses rapidly to potentially lethal levels.[4] Desaturation during anesthetic induction is especially rapid in premature babies, infants, and young children,[5–7] as well as in obese children[8] and those suffering from upper respiratory infection.[9] Obtaining Pa_{O_2} values from arterial blood samples are not helpful in such situations because analysis takes far too long, and securing the airway rather than obtaining arterial blood is the appropriate priority. During a crisis, having a reliable estimate of time remaining before hypoxemia becomes critical would help guide management. For example, it would be perfectly reasonable to again attempt intubation knowing that several minutes remained before desaturation, whereas some other ventilation strategy might be more appropriate if only 30 s remained.

Recently, Masimo Corporation (USA) developed a novel continuous and noninvasive measurement called the Oxygen Reserve Index (ORI). The ORI is a nondimensional index that ranges from 1 (much reserve) to 0 (no reserve) and is measured by optically detecting changes in Sv_{O_2} after Sa_{O_2} saturates to the maximum (see appendix). At this time, the device is not cleared in the United States and is limited to investigational use.

In this pilot study, we tested the hypothesis that the ORI provides a clinically important warning of impending arterial desaturation in pediatric patients during induction of anesthesia. Our primary outcome was the time that elapsed between activation of the Oxygen Reserve alarm until saturation reached 98% without ventilation, that is, the warning time the index provided of impending desaturation.

Materials and Methods

After obtaining approval from the institutional review board (University of Texas Southwestern, Dallas, Texas), we obtained written informed consent from the parents of 33 pediatric patients and assent from 8 patients older than 10 yr. This prospective cohort study was conducted at Children's Medical Center in Dallas, Texas with patients enrolled during a 4-month period extending from January to April, 2014.

Inclusion criteria were pediatric surgical patients with American Society of Anesthesiologists physical status I and II, scheduled for general anesthesia with orotracheal intubation. We excluded patients with substantial cardiorespiratory compromise and those with known or anticipated difficult intubation.

Anesthesia was induced with 8% sevoflurane in 100% O_2 supplemented by intravenous propofol (2 to 3 mg/kg) and fentanyl (1 to 2 μg/kg). Muscle relaxants were not used. After patients became apneic, the trachea was intubated, and the endotracheal tube position was confirmed by the end-tidal carbon dioxide response to a single tidal volume breath. The anesthesia circuit was then disconnected to eliminate apneic oxygenation, and saturation was allowed to decrease to 90%. Subsequently, the anesthesia circuit was reconnected, and patients were ventilated with 100% oxygen until Sp_{O_2} returned to 99 to 100%. Thereafter, anesthesia continued per routine.

The ORI and the Sp_{O_2} were measured simultaneously at 1-s interval with a pulse co-oximeter sensor (R1 25L) placed on the patient's toe and connected to a Radical-7 pulse oximeter (Masimo, USA). The monitor averaging time was set at 8 s, per the manufacturer's default.

The Radical-7 pulse monitor, used for this study, was equipped to collect optical raw data needed to compute ORI but was not equipped to display it. Throughout the study, investigators were, thus, aware of oxygen saturation but not the ORI values that were subsequently provided to the investigators by the manufacturer after offline analysis of the collected raw data. The time at which the ORI alarm would have started was also calculated offline using the manufacturer's proprietary algorithm. Alarm activation was based on the fractional rate of change in ORI rather than on a specific oxygen reserve value. The alarm stopped when the ORI reached its minimal value of 0.

The ORI and Sp_{O_2} values were recorded from a Masimo Pulse Co-Oximeter Sensor at the beginning of apnea, beginning and end of intubation, beginning and end of the Oxygen Reserve alarm, and 2 min after reoxygenation. The beginning of induction (mask application) was designated elapsed time 0. The ORI was also recorded when Sp_{O_2} decreased to 98 and 90% or recovered from 90 and 98%. We also recorded the total apnea time defined as the time from the beginning of apnea until Sp_{O_2} reached 90% and ventilation was reinstated. The early warning time was defined from the beginning of the rapid decrease of the oxygen reserve values (indicated by the start of the ORI alarm), until saturation reached 98%.

Statistical Analysis

The warning time is presented a as median warning time (interquartile range [IQR]) and 95% CI for mean, whereas the rest of the results are presented as mean ± SDs. SAS 9.3 software (SAS Institute Inc., USA) was used to conduct the analyses.

Results

Thirty-three patients were enrolled. Eight resumed spontaneous ventilation during the study period and therefore did not reach the target Sp_{O_2} of 92%. Therefore, these eight were excluded from analysis, leaving 25 patients whose results we report. Demographic and morphometric characteristics

Table 1. Patient's Demographics (N = 25)

Age (yr)	7.6 ± 4.6
Gender (male/female)	11/22
Weight (kg)	32 ± 22
Height (cm)	132 ± 31
BMI (kg/m^2)	20 ± 6

BMI = body mass index.

of the participating patients are presented in table 1. All patients had a Spo_2 of 100% at the beginning of the apneic period.

The induction time (from the beginning of induction with mask application until patients became apneic) was 3.7 ± 1.9 min. Thereafter, the ORI slowly and progressively decreased over a mean of 5.9 ± 3.1 min from 0.73 ± 0.2 at the beginning of apnea to 0.4 ± 0.1 when the ORI began to decrease rapidly. Spo_2 remained 100% throughout this initial period (fig. 1).

Concurrently with alarm activation, the ORI began to decrease rapidly, and in median of 31.5 s (IQR, 19 to 34.3 s), saturation decreased to 98%. Thus, the alarm would have provided a median of 31.5 s (IQR, 19 to 34.3 s; 95% CIs for mean, 23.4 to 60.2 s) warning of impending desaturation had the system been working in real time. The mean (SD), median (IQR), and 95% CI for mean data at all study times are presented in table 2. Among 22 of the 25 patients included in our analysis, the warning time was between 0 and 50 s. The remaining three patients' warning times were at 98, 112, and 221 s (fig. 2).

After reinstitution of ventilation, Spo_2 values continued to decline to a mean saturation of 88 ± 3% before recovering to a Spo_2 of 98% 34 ± 65 s later. The oxygen saturation nadir was 84 ± 2% (table 3).

The ORI was at its minimum value (0) when oxygen saturation was less than 98% and increased rapidly to 0.5 ± 0.3 as saturation increased to 99% and above during reoxygenation.

Mean blood pressures and heart rates at baseline, end of intubation, and at reoxygenation are presented in table 2, along with end-tidal Pco_2 at the end of intubation and at reoxygenation.

Discussion

Pulse oximetry provides continuous, noninvasive assessment of arterial oxygen saturation and is a sensitive detector of hypoxemia[10] and major hypoxic events.[11] However, oxygen supplementation delays detection of hypoventilation by pulse oximetry in both adults[12,13] and children[14] because oxyhemoglobin saturation remains 100% over a wide range of oxygen partial pressures exceeding about 80 mmHg.[15]

For the same reason, it is difficult to predict when desaturation will start in apneic preoxygenated patients. For example, our patients maintained 100% oxygen saturation for an average of more than 6 min of apnea, which is consistent with previous clinical[16,17] reports and computational models.[4] However, there was a substantial variability among patients, which means that in any individual, it would have been difficult or impossible to predict just when the rapid desaturation phase would begin.

Our major finding is that monitoring the ORI before and during intubation detected impending desaturation in median of 31.5s (IQR, 19 to 34.3 s) before noticeable changes in Spo_2 occurred. This represents a clinically important warning time that might give clinicians time for corrective actions. We are unaware of any other method that reliably provides warning that desaturation is imminent.

The ORI is a novel pulse oximeter–based nondimensional index that ranges from 1 to 0 as Pao_2 decreases from about 200 to 80 mmHg. The ORI is based on the Masimo Rainbow SET technology in which the pulsatile signal is

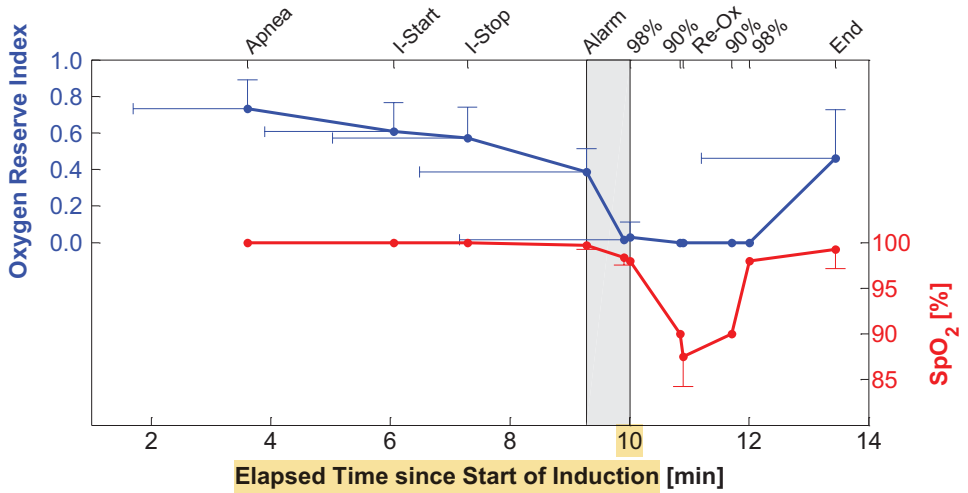

Fig. 1. The Oxygen Reserve Index and Spo_2 values at different times of study. I-Start = beginning of intubation; I-Stop = end of intubation; Alarm = start of the Oxygen Reserve alarm; Re-Ox = reoxygenation; End = end of recording. The *points* and *error bars* represent mean (SD) values.

Table 2. The Oxygen Reserve Index (ORI) Mean, Median, and CI of Means Times at Various Study Times

	Time (min)			Delta Time (min)	Oxygen Reserve Index
	Mean ± SD	Median (IQR)	95% CI for Mean		
Start of apnea	3.7 ± 1.9	3.1 9 (2.7–3.7)	2.9–4.5	N/A	0.73 ± 0.16
Start of intubation	6.3 ± 1.9	5.8 (5.1–6.7)	5.5–7.1	2.6 ± 1	0.60 ± 0.16
End of intubation	7.5 ± 2	6.9 (6.3–8.3)	6.7–8.3	1.2 ± 0.5	0.56 ± 0.17
ORI alarm start	9.6 ± 2.4	9.9 (7.9–10.7)	8.6–10.6	2.1 ± 1.6	0.37 ± 0.11
ORI alarm stop	10.2 ± 2.4	10.3 (8.3–11.4	9.2–11.2	0.6 ± 0.7	0.01 ± 0.6
98% Spo_2 (desaturation)	10.3 ± 2.5	10.3 (8.6–11.7)	9.3–11.3	0.1 ± 0.2	0.03 ± 0.8
90% Spo_2 (desaturation)	11.2 ± 2.4	11.2 (9.6–12.5)	10.2–12.1	0.9 ± 0.6	0.00 ± 0.0
Reoxygenation	11.2 ± 2.4	11.2 (9.6–10.5)	10.2–12.2	0.1 ± 0.3	0.00 ± 0.0
90% Spo_2 (reoxygenation)	11.7 ± 2.2	11.5 (10.3–12.7)	10.5–13.0	0.3 ± 0.3	0.00 ± 0.0
98% Spo_2 (reoxygenation)	12 ± 2.2	11.5 (10.3–12.7)	10.7–13.3	0.3 ± 0.8	0.00 ± 0.0
2 min after reoxygenation	13.5 ± 2.3	13.2 (12.1–14.5)	12.1–14.7	1.4 ± 1.1	0.46 ± 0.26

Delta time: time from one study time measurement to the next.
IQR = interquartile range; N/A = not applicable; Spo_2 = oxygen saturation.

extracted, enabling detection of changes in Pao_2 relative to the changes in Svo_2 at the measurement site. The ORI algorithm combines the Fick principle with the absorption properties of both arterial and venous hemoglobin wavelength. Specifically, as Pao_2 increases beyond 100 mmHg, Svo_2 continues to increase, even though Sao_2 has effectively saturated at 100%. This modest increase in Svo_2 above its normal value of approximately 75% will eventually stop as Pao_2 reaches significantly higher values (*i.e.*, more than 200 mmHg). The consequent wavelength change makes it possible to detect changes in Pao_2 up to about 200 mmHg if not even higher.

Potential confounding factors include oxygen consumption, cardiac output, blood pH, Pco_2, temperature, the amount of perfusion (venous pulsation), and the presence of abnormal hemoglobins. For a more detailed explanation of the relationship between pulse oximetry and ORI, see appendix.

The ORI was validated in an institutional review board–approved study conducted by Masimo per ISO-80601 guidelines (not peer reviewed or published)[18] in 11 adult volunteers who underwent a variety of interventions to change their Pao_2 and Spo_2 levels. A total of 1,885 paired sets of ORI and Pao_2 values were collected. An index of 0.3 provided more than or equal to 80% specificity for a Pao_2 less than 150 mmHg. Although we did not evaluate Pao_2, our results suggest a consistent and clinically useful relationship between the ORI and blood partial pressure of oxygen.

This being the initial report about the ORI, there remain many questions that will have to be addressed in future studies. For example, we did not evaluate the oxygen index in the setting of abnormally high oxygen consumption states such as fever or hypermetabolic stress. We expect that the relationship between Pao_2 and ORI will remain similar, but that the "warning time" will be reduced because Pao_2 will decrease more rapidly during apnea. More importantly, we did not evaluate the correlation between ORI and Pao_2, which remains of obvious clinical interest.

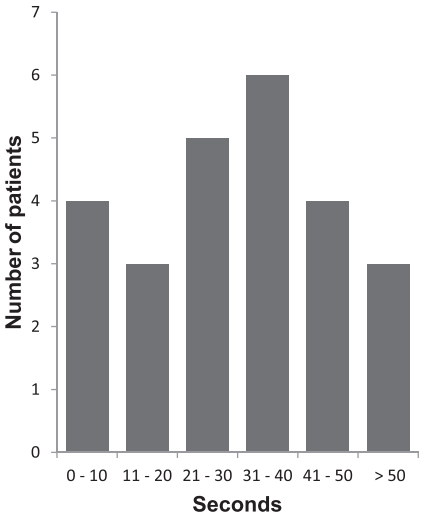

Fig. 2. The early warning time distribution. The early warning time (seconds) was defined from the beginning of the rapid decrease of the oxygen reserve values (indicated by the start of the Oxygen Reserve Index alarm), until saturation reached 98%. Twenty-two of 25 patients had warning times between 0 and 50 s. The remaining three patients' warning times were at 98, 112, and 221 s.

Furthermore, all our patients were preoxygenated before apnea was instituted, and ORI values were recorded. Thus, it is probable that at lower Fio_2 (room air), the warning time will be significantly shorter. Future studies will also have to quantify the accuracy or reliability of ORI and the extent to which hemodynamic and other common clinical perturbations might influence the index.

The ORI measurements were obtained from a pulse oximeter sensor placed on the patient's toe. Thus, sensor placement in other sites might provide different advanced warning times. Our study group was too small to permit evaluating the relationship between the ORI, age, and

Table 3. The Oxygen Reserve Index (ORI) and Oxygen Saturation (Spo_2) Values, Hemodynamic Data, and End-tidal Carbon Dioxide at Various Study Times

	Spo_2 (%)	Heart Rate (beats/min)	Mean Blood Pressure (mmHg)	End-Tidal CO_2 (mmHg)
Start of intubation	99.9 ± 0.1			
End of intubation	99.9 ± 0.2	117 ± 25	59 ± 12	28 ± 4
ORI alarm start	99.7 ± 0.5			
ORI alarm stop	98.4 ± 0.8			
98% Spo_2 (desaturation)	98.0 ± 0.0			
90% Spo_2 (desaturation)	90.0 ± 0.0			
Reoxygenation	87.3 ± 3.1	109 ± 24	54 ± 7	46 ± 7
90% Spo_2 (reoxygenation)	90.0 ± 0.0			
98% Spo_2 (reoxygenation)	98.0 ± 0.0			
2 min after reoxygenation	99.2 ± 2.1			

weight. But although both likely influence the duration of apnea that can be maintained with full saturation, neither seems likely to directly influence accuracy of the ORI, any more than pulse oximetry is much influenced by morphometric and demographic characteristics.

We evaluated the ORI in one clinical scenario, but believe that warning of impending desaturation is likely to also prove useful during airway maneuvers (suctioning, bronchoscopy, *etc.*) in critically ill patients. The ORI may also be helpful for assessing the effectiveness of preoxygenation before rapid sequence induction and in avoiding hyperoxia in neonates.

In conclusion, most intubations—fortunately—are rapid and smooth. But when they are not, clinicians need to make life-sustaining strategic decisions. In this pilot study, we found that during prolonged apnea in healthy anesthetized children, the ORI detected impending desaturation in median of 31.5 s (IQR, 19 to 34.3 s) before noticeable changes in Spo_2 occurred. Knowing even roughly how much time remains before the rapid desaturation phase begins seems likely to guide proper decisions.

Acknowledgments

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Competing Interests

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Appendix: Relationship between Pulse Oximetry and ORI

The Fick principle[19] relates oxygen consumption (Vo_2) with cardiac output (CO) and oxygen content of arterial blood (Cao_2) and deoxygenated venous blood (Cvo_2).

$$Vo_2 = CO \times (Cao_2 - Cvo_2).$$

The oxygen content equation for arterial (Cao_2) and venous (Cvo_2) blood is given by

$$Cao_2 = (Sao_2 \times tHb \times 1.34) + 0.003 \times (Pao_2)$$

$$Cvo_2 = (Svo_2 \times tHb \times 1.34) + 0.003 \times (Pvo_2),$$

where tHb is total hemoglobin.

Substituting the oxygen content equation for the arterial (Cao_2)[20] and venous (Cvo_2) blood, we are left with the following equation (where Svo_2 is the oxygen saturation in the venous blood and Pvo_2 is the partial pressure of oxygen in the venous blood):

$$Vo_2 = CO \times \left[\left((Sao_2 \times tHb \times 1.34) + 0.003 \times Pao_2\right)\right] - \left[\left((Svo_2 \times tHb \times 1.34) + 0.003 \times Pvo_2\right)\right].$$

This equation can be modified *via* oxygen saturation equations to the following format:

$$Vo_2 = CO \times (1.34 \times tHb \times (Sao_2 - Svo_2) + 0.003 \times (Pao_2 - Pvo_2)). \quad (1)$$

The oxygen dissociation curve provides a relationship between Sao_2 and Pao_2 as given by the equation below.

$$Sao_2 = f(Pao_2) \text{ and } Svo_2 = f(Pvo_2). \quad (2)$$

Substituting equation 2 in equation 1, we get:

$$Vo_2 = CO \times \left[1.34 \times tHb \times \left(f(Pao_2) - Svo_2\right) + 0.003 \times \left(Pao_2 - f^{-1}(Svo_2)\right)\right].$$

Hence, for a constant oxygen consumption and cardiac output, Svo_2 is directly proportional to Pao_2, as f (defined in eq. 2) is an increasing function. This results in the following relationship:

$$Svo_2 \propto Pao_2 \text{ for constant } Vo_2,\ CO. \quad (3)$$

Pulse oximeters work by measuring the absorption of pulsatile blood at the measuring site (finger). Pulsatile changes are observed at the arteries, capillaries, and in the venules, although to a lesser degree in the venules. A pulse oximeter absorption measurement at wavelength λ, denoted by $A(\lambda)$, is thus affected by both arterial and venous blood absorption changes.

$$A(\lambda) = A_a(\lambda) + \alpha A_v(\lambda), \quad (4)$$

where $\alpha << 1$ and α is dependent on perfusion at the measurement site.

In the absence of dyshemoglobins:

$$A_a(\lambda) = Sao_2 \times A_a^{O_2Hb}(\lambda) + (100 - Sao_2) \times A_a^{HHb}(\lambda) \quad (5)$$

$$A_v(\lambda) = Svo_2 \times A_v^{O_2Hb}(\lambda) + (100 - Svo_2) \times A_v^{HHb}(\lambda) \quad (6)$$

where $A_a^{O_2Hb}$ is the absorption of oxyhemoglobin in arterial blood, $A_v^{O_2Hb}$ is the absorption of oxyhemoglobin in venous blood, A_a^{HHb} is the absorption of deoxyhemoglobin (reduced) in arterial blood, and A_v^{HHb} is the absorption of deoxyhemoglobin (reduced) in venous blood.

Substituting equations 5 and 6 into equation 4:

$$\begin{aligned} A(\lambda) = {} & (Sao_2 \times A_a^{O_2Hb}(\lambda) + (100 - Sao_2) \\ & \times A_a^{HHb}(\lambda)) + \alpha\,(Svo_2 \times A_v^{O_2Hb}(\lambda) \\ & + (100 - Svo_2) \times A_v^{O_2Hb}(\lambda)). \end{aligned} \quad (7)$$

Combining equation 3 and equation 7, we observe that $A(\lambda)$ changes as a function of Pao_2.

The units of measurement for the different components in the equations are as follows:

- Sao_2, Svo_2 = percent saturation expressed as decimal fraction (*e.g.*, 0.98).
- tHb is measured in g/dl.
- Pao_2 and Pvo_2 are expressed in mmHg.
- Cardiac output is expressed in ml/min.
- Vo_2 is expressed in ml/min.

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