Oxygen reserve index, a new method of monitoring oxygenation status: what do we need to know?

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Abstract

The oxygen reserve index (ORI) is a new technology that provides real-time, non-invasive, and continuous monitoring of patients' oxygenation status. This review aimed to discuss its clinical utility, prospect and limitations. A systematic literature search of PubMed, MEDLINE, Google Scholar, and ScienceDirect was performed with the keywords of "oxygen reserve index," "ORI," "oxygenation," "pulse oximetry," "monitoring," and "hyperoxia." Original articles, reviews, case reports, and other relevant articles were reviewed. All articles on ORI were selected. ORI can provide an early warning before saturation begins to decrease and expands the ability to monitor the human body's oxygenation status noninvasively and continuously with the combination of pulse oximetry so as to avoid unnecessary hyperoxia or unanticipated hypoxia. Although the technology is so new that it is rarely known and has not been applied to routine practices in hospitals, it shows good prospects for critical care, oxygen therapy, and intraoperative monitoring.

Keywords: Oxygen reserve index (ORI); Oxygenation; Pulse oximetry; Monitoring; Hyperoxia

Introduction

The oxygen status of arterial blood is generally classified into 3 categories: hypoxia (less than normal oxygenation, partial pressure of oxygen [PaO_2]: 0–80 mmHg), normoxia (normal oxygenation, PaO_2: 81–100 mmHg) and hyperoxia (higher than normal oxygenation, $PaO_2 > 100$ mmHg). Although there are no unified standards, hyperoxia is roughly subdivided into mild hyperoxia (PaO_2: 101–200 mmHg) and severe hyperoxia ($PaO_2 >$ 200 mmHg).[1] Some researchers divide hyperoxia into three subcategories: mild (PaO_2: 100–199 mmHg), moderate (PaO_2: 200–299 mmHg), and severe ($PaO_2 >$ 300 mmHg).[2] PaO_2 of 100 to 200 mmHg is particularly notable in mild hyperoxia. At this range, the patient's oxygenation status is slightly above normoxia, which enriches the body with oxygen but does not pose additional risk or harm from high PaO_2 described in many reports; contrarily, it is associated with lower mortality.[3,4] Consequently, an excess PaO_2 of approximately 100 mmHg can be regarded as the oxygen reserve in the human body corresponding to the original description of the oxygen reserve index (ORI) by Scheeren *et al*.[1]

Both hypoxia and normoxia can be assessed noninvasively and continuously using pulse oximetry, the assessment of hyperoxia predominantly relied on the invasive and intermittent arterial blood gas analysis (aBGA) before the introduction of ORI. ORI is a dimensionless index with scores ranging from 0 to 1 at PaO_2 from approximately 100 to 200 mmHg, which reflects the oxygenation status of mild hyperoxia.[1,5-7] At present, although the detection of severe hyperoxia still depends on invasive methods of monitoring, ORI can evaluate a part of the hyperoxic range noninvasively.

How is Oxygen Reserve Index Recorded?

In the hypoxia and normoxia range ($PaO_2 \leq 100$ mmHg), the pulse oxygen saturation (SpO_2) can be evaluated using pulse oximetry. When PaO_2 exceeds 100 mmHg, arterial oxygen saturation (SaO_2) reaches 100% and then remains unchanged, but mixed venous oxygen saturation (SvO_2) keeps rising. The change in SvO_2 changes the absorption of the incident light, thus changing the signals measured with the increase in PaO_2. These signals can be extracted with Masimo Rainbow Signal Extraction Technology. In addition, an increase in PaO_2 beyond approximately 200 mmHg allows SvO_2 to reach a plateau as well.

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Consequently, ORI is recorded by optically detecting the changes in SvO_2 after SaO_2 reaches maximum saturation and before SvO_2 reaches maximum saturation. More specifically, ORI is sensitive to the changes in PaO_2 with the range of 100 to 200 mmHg.[1]

Correlation Between Oxygen Reserve Index and PaO_2

Changes in ORI scores within 0–1 can indirectly reflect the changes in PaO_2 within 100 to 200 mmHg. Although ORI and PaO_2 do not show one-to-one correspondence, they positively correlate within the aforementioned ranges.

A regression analysis showed a stronger correlation between ORI and PaO_2 at $PaO_2 \leq 240$mmHg ($r^2 = 0.536$) than at $PaO_2 \geq 240$ mmHg ($r^2 = 0.0016$). Based on this finding, researchers concluded that there is a positive correlation between ORI and PaO_2 at $PaO_2 \leq 240$ mmHg but that there is no correlation between ORI and PaO_2 at $PaO_2 > 240$ mmHg. At $PaO_2 > 100$ mmHg, all ORI scores were over 0.24; at $PaO_2 > 150$ mmHg, ORI scores were over 0.55 in 96.6% of the samples. These findings suggest that ORI > 0.24 manifests $PaO_2 \geq 100$ mmHg. Similarly, an ORI score of 0.55 appears to be the lower threshold for $PaO_2 > 150$ mmHg.[8]

Various Oxygenation Monitoring Methods

Pulse oximetry

Pulse oximetry provides continuous, non-invasive, and real-time monitoring of SpO_2. However, the range of detection is limited to 0 to 100 mmHg, and it fails to indicate the downward trend in PaO_2 before saturation begins to plummet.[9,10]

Blood gas analysis (BGA)

BGA is the gold standard method to measure oxygenation using PaO_2. However, it is invasive, mostly intermittent, and occasionally delayed.[11] Recently, continuous intra-arterial BGA has been introduced.[12-14] However, it is relatively impractical for real-time, point-of-care assessments.

Oxygen reserve index

ORI is a novel, continuous, non-invasive, and real-time parameter to assess PaO_2 levels in the range of 100 to 200 mmHg. It provides real-time oxygenation monitoring and indicates the downward trend of PaO_2, thus alarming clinicians early of the changes in the oxygenation status [Table 1].[1,5-7]

Clinical Benefits of ORI

Early warning for desaturation

In a pilot study involving 25 children who had undergone general anesthesia after endotracheal intubation, researchers from the University of Texas Southwestern and Children's Medical Center found that ORI assisted clinicians in identifying imminent changes 31.5 s (median; interquartile range, 19.0–34.3 s) before the occurrence of a noticeable drop in SpO_2.[6] In another study involving 16 adults who had undergone rapid-sequence induction of general anesthesia before endotracheal intubation, researchers from the Fukushima Medical University School of Medicine also found that ORI could predict a hypoxic state approximately 30 s before the decline in SpO_2.[7] Moreover, a validation study involving healthy and conscious volunteers with spontaneous breathing clearly showed that a decline in ORI occurred well before the changes in SpO_2.[15] In 2018, a study in Japan found that ORI decreased earlier than SpO_2 during one-lung ventilation (OLV),[16] and in 2019, Spanish anesthesiologists declared that ORI predicts hypoxemia during OLV.[17] In addition to these prospective clinical studies, case reports support the role of ORI in early alarm for oxygenation deterioration as well.[18,19] Collectively, the aforementioned studies using different methods and objects demonstrate that ORI predicts desaturation in anesthesia induction and surgery under general anesthesia and awake conditions, in double- and single-lung ventilations, and in adults and children.

In the oxyhemoglobin dissociation curve, the relationship between PaO_2 and SaO_2 is not linear. In other words, when PaO_2 is greater than 80 mmHg, SaO_2 may continue to be greater than 95%. Nevertheless, once PaO_2 decreases to less than 70 mmHg, SaO_2 declines rapidly. This physiological phenomenon is called "slippery slope."[9] Sudden occurrence of "slippery slope" is undoubtedly a huge challenge for unprepared clinicians. In view of this, pulse oximetry alone is a late detector of hypoxia. Fortunately, "slippery slope," the enemy that lies in the shadows and can attack the patients at any time, can now be detected 30 s ahead via ORI. Within 30 s, clinicians can make the right decision and respond quickly before rapid

Table 1: Comparison among SpO_2, BGA, and ORI on monitoring oxygenation status.

Items	Pulse oximetry	BGA	ORI
Continuity	Continuous	Continuous/Intermittent	Continuous
Trauma	Non-invasive	Invasive	Non-invasive
Timeliness	Real-time	Occasionally delayed	Real-time
PaO_2 range	0–100 mmHg	No limit	100–200 mmHg
Oxygenation status	Hypoxia/Normoxia	Hypoxia/Normoxia/Hyperoxia	Mild Hyperoxia
Cost	Cheap	Costly	–

SpO_2: The oxygen saturation; BGA: Blood gas analysis; ORI: Oxygen reserve index; "–": Not available.

desaturation begins so as to avoid hypoxemia-related complications. This is definitely not an overstatement. A case report revealed that doctors accidentally discovered the discontinuation of the oxygen supply through ORI.[19] Therefore, the sharp decline in ORI with an unchanged trend of SpO_2 should attract the doctor's attention and vigilance.

Although there are still no reports on the application of ORI in the intensive care unit (ICU), we have every reason to believe that ORI can play an important role in the early warning of desaturation for critically ill patients with acute respiratory failure or other conditions in the ICU. And another entity that deserves to be highlighted is the ORI alarm. However, this alarm activation was predominantly based on the real-time fractional rate of change in ORI rather than on the specific oxygen reserve.

ORI in oxygen therapy

Oxygen supplementation has a widespread and essential application in the perioperative and ICU settings to prevent potential hypoxia-related damage. Hypoxia is easily noticed with the application of pulse oximetry, but its diagnosis depends on BGA, which is invasive and intermittent. Usually, doctors are well-concerned about hypoxia and worry that patients will approach "slippery slope"; therefore, they treat patients with high-flow oxygen. As a result, non-anoxic patients who do not require oxygen therapy are supplemented with excess oxygen, and hypoxic patients are supplemented with inappropriately high concentrations of oxygen. In fact, unnecessary oxygen prescriptions to non-hypoxic patients are a common mistake in respiratory care.[20-23]

Scientific evidence suggests that supplemental oxygen leading to hyperoxia may have potential risks in various clinical situations,[24-27] including deleterious effects on the cardiovascular system, such as systemic vasoconstriction and decrease in the cardiac output and coronary flow, which may result in myocardial infarction,[28-30] nervous system, such as reduction in the cerebral blood flow,[31] and respiratory system, such as atelectasis and increased intrapulmonary shunting, *etc*.[32] Especially, in critically ill patients, many studies reported a significant correlation between increased mortality and hyperoxia.[2-4,33-36] However, hyperoxia is not always harmful. As mentioned, mild hyperoxia seems to be relatively safe. Recent studies found that the probability of in-hospital deaths Table 1 showed its lowest values at PaO_2 values within 110 to 160 mmHg.[3,4]

Attention should be increased on the dangers of prolonged hyperoxia since the harms of severe hyperoxia and hypoxia are well-recognized by all clinicians,[37] and the need for a more precise oxygen therapy is increasing. As we already know, the range for PaO_2 monitored using pulse oximeter is limited to 0 to 100 mmHg while that monitored using ORI is limited to 100 to 200 mmHg. Both methods are non-invasive, continuous, and real-time. Therefore, we could infer that ORI in conjunction with pulse oximetry can extend the real-time, continuous, and non-invasive visibility of a patient's oxygenation status up to a PaO_2 of 0 to 200 mmHg, which could not be previously monitored.

Table 2: Comparison of visibility among different methods.

Non-invasive method	Range of PaO_2 (mmHg)
Pulse Oximetry	$0 \leq PaO_2 \leq 100$
ORI	$100 < PaO_2 \leq 200$
Pulse Oximetry with ORI	$0 \leq PaO_2 \leq 200$

ORI: Oxygen reserve index.

Theoretically, the application of ORI could change the visibility of the patient's oxygenation status [Table 2].[1]

Thus, clinicians may assess patients' oxygenation status more accurately and control the titration of FiO_2 more precisely, without BGA to prevent unexpected hypoxia or unintended hyperoxia in the ICU, operating room, or ward. Recently, a case reported in India successfully demonstrated this clinical value of ORI. FiO_2 was titrated to 0.4 to 0.5 to maintain an ORI score between 0 and 0.3 and SpO_2 above 97% in a neonate undergoing re-exploration of a tracheoesophageal fistula to avoid excessive oxygenation while maintaining a marginal oxygen reserve.[38] On the other hand, Keisuke Yoshida *et al*[39] validated the important role of ORI to avoid excessive hyperoxia during general anesthesia by adjusting ORI.

ORI in preoxygenation

Preoxygenation is a universal procedure performed before general induction and endotracheal intubation worldwide to increase the patient's oxygen stores and prolong the duration of safe apnea oxygenation.[40-42] Additionally, preoxygenation is a standard technique in general anesthesia but is frequently neglected. With the application of pulse oximetry alone as a monitoring tool, doctors cannot guarantee that the patient's PaO_2 would be greater than 100 mmHg or that the intrapulmonary oxygen would keep increasing, as anticipated. Particularly, in obese or critically ill patients, the common methods of 3 min of tidal breathing, four deep breaths within 30 s, or eight deep breaths within 60 s may not achieve high-quality preoxygenation.[43,44] Therefore, ORI may assist us in identifying unsuccessful preoxygenation. As aforementioned, ORI > 0.24 indicates $PaO_2 \geq 100$ mmHg, and ORI > 0.55 appears to be the lower threshold to indicate $PaO_2 \geq 150$ mmHg.[5] During preoxygenation, if the ORI scores do not show an upward trend and stay relatively low and even if SaO_2 has reached 100%, it is necessary to perform further interventions, such as positive-pressure ventilation, continuous positive airway pressure, positive end-expiratory pressure, bi-level positive airway pressure, and high-flow nasal oxygen.[45,46] However, although ORI could approach the respiratory management individualized in theory, it is regrettable that there has been no relevant clinical study to confirm this point.

Influence of Indigo Carmine on ORI

Indigo Carmine is a blue dye that is generally regarded as safe and biologically inactive. It is rapidly excreted in the

urine and routinely administered intravascularly during urologic and gynecologic procedures to localize the ureteral orifices and to identify severed ureters and fistulous communications.[47] The effects of indigo carmine on SpO_2, hemoglobin, and regional cerebral saturation have been reported.[48-50]

Recently, a retrospective study demonstrated that the intravenous injection of indigo carmine could greatly influence the ORI score. In all 19 patients evaluated in this retrospective study, ORI decreased rapidly after the intravenous injection of indigo carmine, and in 10 of the 19 patients, it was reduced to 0. The median lowest ORI score was 0 (range: 0–0.16), and the median time to reach the lowest ORI score was 2 min (range: 1–4 min) after indigo-carmine injection. Furthermore, ORI scores returned to the pre-injection level within 20 min in 13 of the 19 patients, and the median time to return to the pre-injection level was 10 min (range: 6–16 min).[51]

Indigo Carmine is a water-soluble dye with a 4 to 5-min half-life after its intravenous injection, and its peak light absorption is at 620 nm.[52] The close numerical value of the wavelength of the ORI recording to the absorbance of indigo carmine may explain the effects of indigo carmine on ORI.[51] In other words, the desaturations are artificial, and the rapid decrease in ORI does not indicate real hypoxia in patients. A transient decrease in ORI scores during urologic or gynecologic surgery is not a cause of panic. We should first verify if indigo carmine was used intravascularly.

In addition, except for indigo carmine, indocyanine green and methylene blue can disturb the measurement recorded with pulse oximeter.[52,53] Moreover, an interference of cerebral near-infrared oximetry by bilirubin has been reported in patients with icterus,[54] and with the increasing incidence of tumors, fluorescence-guided surgery is increasingly being used for tumor resection. Therefore, despite the lack of relevant clinical studies, we should consider the potential interference of various dyes and lights in the ORI measurements.

The greatest limitation of ORI at this stage is that the technology is too new. There seems to be a dearth of evidence for the useful application of ORI. Although ORI has been validated for several clinical utilities, it does not answer all the questions perfectly yet.[55] Naturally, clinicians might think, "Does this stuff really work? It looks like a toy, not a tool."[56] Indeed, new things are always doubted, as Saugel said, there are no definite answers. Although ORI has a broad application in theory and good application in prospect, its evidence is insufficient. Therefore, we need more high-quality clinical studies on the clinical value of ORI.

Regardless of the original disease, the patient's death had ultimately resulted from lack of oxygen delivery to the brain or heart. Therefore, monitoring and treatment of supplemental oxygen is a race against time. Obviously, ORI is an important tool assisting us to win this race, as it provided clinicians with valuable time of approximately 30 s in advance to correctly respond to the impending hypoxia and to save the patient's life.

In addition, ORI enables clinicians to assess a patient's oxygenation status more accurately without the application of BGA, which avoids unnecessary hyperoxia and unexpected hypoxia to a large extent. However, we must pay close attention to patients who have been intravenously injected with dyes or lights, which would interfere with the ORI measurement. Studies are underway on the application prospect of ORI in various settings. This new technology could provide us with new discoveries in physiology and pathophysiology and open new horizons in the monitoring and treatment of patients.

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Conflicts of interest

None.

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