

Usefulness of oxygen reserve index (ORi) in clinical practice

Użyteczność indeksu rezerwy tlenowej (ORi) w praktyce klinicznej

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Słowa kluczowe: monitorowanie, hipoksja, indeks rezerwy tlenowej, hiperoksja, tlenoterapia.

Abstract

Oxygen is the most common and widely used drug. Oxygen therapy is used not only among mechanically ventilated patients in intensive care units, but also in the perioperative period and in patients requiring oxygen supplementation in other hospital wards. The main methods of monitoring the blood oxygenation level include arterial blood gases and pulse oximetry. A new parameter that allows the monitoring of patients' oxygenation status is the oxygen reserve index (ORi). The ORi provides easy, non-invasive, bedside monitoring of oxygen reserve capacity. The oxygen reserve index reflects the partial pressure of oxygen in arterial blood (PaO₂) in the range 100–200 mm Hg. It therefore allows the detection of mild hyperoxia, enabling the safe use of lower concentrations of oxygen in the breathing mixture. It is also a useful tool in predicting impending hypoxia. This paper summarizes the usefulness of oxygen reserve index monitoring in various clinical situations in everyday anaesthesiology practice.

Streszczenie

Tlen jest najczęściej i najpowszechniej używanym lekiem. Tlenoterapia stosowana jest wśród wentylowanych mechanicznie pacjentów oddziałów intensywnej terapii, w okresie okołoperacyjnym, a także u pacjentów wymagających suplementacji tlenem, przebywających na innych oddziałach szpitalnych. Do głównych metod monitorowania poziomu utlenowania krwi w organizmie należą oznaczanie gazometrii krwi tętniczej oraz pulsoksymetria. Nowym parametrem pozwalającym na monitorowanie gospodarki tlenowej jest indeks rezerwy tlenowej (ORi). ORi umożliwia łatwe, nieinwazyjne, przyłóżkowe monitorowanie poziomu rezerwy tlenowej organizmu. Indeks rezerwy tlenowej odzwierciedla wartości ciśnienia parcjalnego tlenu we krwi tętniczej (PaO₂) w zakresie 100–200 mm Hg. Pozwala on na wykrywanie łagodnej hiperoksji, co umożliwia bezpieczne stosowanie niższych stężeń tlenu w mieszaninie oddechowej. Jest również przydatnym narzędziem w przewidywaniu zagrażającej hipoksji. W artykule omówiono przydatność monitorowania indeksu rezerwy tlenowej w różnych sytuacjach klinicznych z codziennej praktyki anestezjologicznej.

Introduction

Blood oxygen saturation level analysis is the primary method of monitoring the efficacy of oxygen treatment. However, measurement of blood saturation (SpO₂) is subject to many errors. In recent years, there have been more and more reports discussing the reliability of not only SpO₂, measured at the periphery, but also a new parameter, which is the oxygen reserve index (ORi).

Oxygen management

Oxygen is an essential element for aerobic animals; however, its elevated tension in the blood can be harmful and can induce several disorders. The partial pressure of atmospheric oxygen at sea-level with atmospheric pressure 760 mm Hg is approximately

159.6 mm Hg, which is equivalent to 21%. However, its partial pressure progressively decreases during the transport to various organs, which is known as the oxygen cascade. There are 6 important points of this cascade ending in the mitochondria (Figure 1).

Physiologically, oxygen tension ranges between 60 and 100 mm Hg in the arterial blood. Hypoxia is a condition when the oxygen content in the tissues is reduced. Hyperoxia is defined as excessive levels of oxygen in the tissues. However, an increase of arterial blood tension to 120–150 mm Hg is well tolerated and frequently accepted as slight hyperoxia, and a blood partial tension of oxygen between 120–200 mm Hg is considered as a mild hyperoxaemia [1–3]. Severe hyperoxaemia with partial oxygen tension above 200 mm Hg is associated with various adverse outcomes, including an increase in mortality linear to

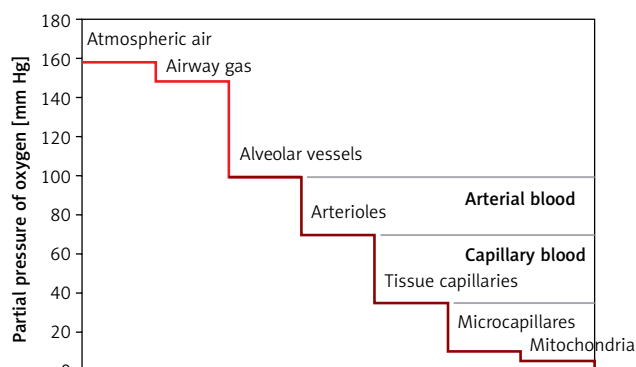


Figure 1. The physiological oxygen cascade

oxygen [4]. An extreme tension of oxygen (greater than 300 mm Hg) has been associated with a dramatic mortality ratio ranging between 59% and 92% in critically ill patients [5]. Hence, maintaining oxygen tension at a physiological value plays a crucial role in patients treated with artificial ventilation. However, a control of oxygen is mainly based on invasive blood gas analysis, and the non-invasive monitoring is not well cascaded, and it is still being studied (Table 1).

Arterial blood gas test

An arterial blood gas (ABG) test is one of the most frequently performed tests in intensive care units (ICU). It is the most accurate method of assessing the oxygenation level by determining the level of oxygen pressure in arterial blood (PaO_2) [6, 7]. The ABG test is used to detect hypoxia (0–80 mm Hg), normoxia (80–100 mm Hg), and hyperoxia (> 100 mm Hg), but it can also be used to measure parameters such as the level of carbon dioxide pressure in arterial blood (PaCO_2), pH, concentration of bicarbonate in arterial blood (HCO_3^-), and excess or deficit of base in arterial blood (BE), thus allowing the assessment of ventilation and the body's acid-base balance [8]. However, continuous measurement of PaO_2 and other gas exchange parameters is not feasible [9]. The commonly used method of blood saturation monitoring is relatively accurate, but it only provides information on changes in arterial blood oxygen pressure within the range 0–100 mm Hg. This means it does not enable early diagnosis of hyperoxia, which is increasingly indicated as a factor in the development of multi-organ complications, including brain function disorders [10, 11]. Therefore, the ABG test, despite its many limitations, remains the gold standard for measuring gas exchange parameters.

Haemoglobin oxygen saturation monitoring – pulse oximetry

Pulse oximetry is a non-invasive method of measuring blood oxygenation. The first blood saturation

sensor (pulse oximeter) was designed in the 1970s by a group of Japanese engineers led by Takuo Aoyagi [12]. Pulse oximetry has since become the standard for monitoring blood oxygenation in a variety of clinical settings. It is a continuous, fast, and relatively accurate method; however, its reliability can be considerably affected by impaired blood perfusion, darker skin pigmentation, or the presence of different types of haemoglobin [13]. Therefore, a growing number of researchers have been paying attention to a new method of monitoring blood oxygen saturation, i.e. the oxygen reserve index (ORi).

Oxygen Reserve Index (ORi)

Monitoring of the ORi is a non-invasive method for diagnosing hyperoxia. The ORi measures the oxygenation reserve status in the mild hyperoxia range, i.e. PaO_2 of 100–200 mm Hg. These values correspond to ORi variations between 0.00 and 1.00, with 0 indicating $\text{PaO}_2 \leq 100$ mm Hg and 1.00 indicating $\text{PaO}_2 \geq 200$ mm Hg. A further increase in PaO_2 above 200 mm Hg does not lead to an increase in the ORi above 1.00. The ORi can provide information on both hyperoxia and impending hypoxia [14].

Similarly to pulse oximetry, the ORi is measured non-invasively in real time by placing a probe on a patient's finger [15].

Created by Masimo Corporation, the sensor for measuring the ORi analyses changes in the absorption of incident light in arterial and venous blood. This enables the measurement of arterial oxygen saturation (SaO_2) and oxygen saturation of mixed venous blood (SvO_2). When PaO_2 exceeds 100 mm Hg during oxygen supplementation, SaO_2 peaks at 100%. In contrast, SvO_2 continues to increase, changing the absorption of incident light, until it reaches a plateau at PaO_2 values of about 200 mm Hg. These changes in SvO_2 in the PaO_2 range of 100–200 mm Hg provide a basis for determining the ORi [14].

Correlation between PaO_2 and oxygen reserve index

The reliability of the ORi in the assessment of moderate hyperoxia has been corroborated in clinical observations. They have documented a close relationship between PaO_2 and the ORi [16, 17]. In the range of moderate hyperoxia (PaO_2 100–200 mm Hg), the relationship between these parameters is strong and allows the determination of the trend of ORi changes depending on changes in PaO_2 [17]. A linear relationship between these 2 variables has been observed to hold up to a PaO_2 of 240 mm Hg; however, when this value was exceeded, linear regression analysis no longer showed such a close relationship. PaO_2 values above 100 mm Hg were found to correspond to an ORi of 0.24, and PaO_2 values equal to or greater than 150 mm Hg corresponded to an ORi above 0.55 [16].

Table 1. Comparison of available methods of monitoring oxygen management

Method	Detection	Range	Invasiveness	Continuity	Advantages/disadvantages
ABG	Hypoxia Normoxia Hyperoxia	No limits	Yes	No	+ The most accurate method + Possibility of measuring other parameters – The need to collect blood samples
SpO ₂	Hypoxia Normoxia	0–100 mm Hg	No	Yes Real-time	+ Commonly accessible – Measurement can be affected by many factors
ORi	Mild hyperoxia	100–200 mm Hg	No	Yes Real-time	+ May warn of impending hypoxia – Measurement can be affected by many factors

ABG – arterial blood gas test, SpO₂ – blood saturation, ORi – oxygen reserve index.

The strong association between the ORi and PaO₂ also enables safe monitoring of patients treated postoperatively with passive oxygen therapy. In patients monitored with the ORi, the assessment of the oxygen dose administered in the postoperative period showed that an oxygen supply of much less than 4 l/min was needed [18].

It is worth noting that ORi monitoring makes it possible to maintain physiological PaO₂ values and thus avoid postoperative hyperoxia. Therefore, it can be suggested that the ORi is highly useful in monitoring and dosing oxygen in patients requiring oxygen supplementation, e.g. in the postoperative period [18].

Prediction of impending hypoxia

The ORi shows high sensitivity in detecting low PaO₂ levels, owing to which it can be used to predict impending hypoxia when SpO₂ values are high and have not yet started to change [17]. A study by Applegate *et al.* showed that a drop in the ORi to near 0.24 could provide an advance warning signal of decreasing PaO₂ when SpO₂ was still at a maximum level [16].

This relationship has been used in clinical practice in the anaesthesia of a newborn with a tracheo-bronchial fistula [19]. Newborns are a particularly demanding group of patients. They are sensitive to both high and low oxygen concentrations. Excess oxygen in the breathing mixture may result in conditions such as retinopathy of prematurity [20]. The use of ORi monitoring in such a sensitive patient made it possible to observe the oxygenation trend, and on its basis to make decisions about the oxygen concentrations to be administered in the breathing mixture. This minimised the risk of hyperoxia and hypoxia, as well as their complications [19].

In their study, Shimizu *et al.* showed that ORi monitoring helped prevent deep desaturation of a one-year-old patient during nasotracheal intubation because the ORi was observed to fall prior to a decrease in SpO₂. In another patient, hospitalised in the ICU due to pulmonary hypertension, desaturation caused

by exacerbation of the disease was prevented owing to the use of the ORi [21].

ORi in predicting hyperoxia

High partial pressure oxygen values are as dangerous for the human body as are low values [22]. Breathing a mixture containing a high concentration of oxygen leads to increased production of reactive oxygen species (ROS) [23]. ROS are produced during oxidative phosphorylation reactions taking place in mitochondria. The electron transport respiratory chain is a complex of proteins and organic molecules located in the inner membrane of mitochondria. All electrons transported in the respiratory chain come from NADH and FADH₂ molecules [24]. Electrons are transferred between the 4 complexes (complexes I–IV) of the respiratory chain during a series of redox reactions. The energy released in these reactions is stored as a proton gradient. It is used to produce ATP in the process of chemiosmosis. Both processes constitute oxidative phosphorylation. From complex IV, electrons are transferred to O₂, which is the final acceptor for electrons [25]. The reduction of oxygen requires 4 electrons, which, when combined with the acceptance of 4 protons, produce 2 water molecules. However, the transfer of 1 or 2 electrons leads to the formation of reactive superoxide ions. ROS, as well as their reaction products, cause oxidation of lipids and proteins, and cause mutations in DNA, and are therefore harmful to cells [26]. However, cells have the ability to neutralize ROS thanks to enzymes such as superoxide dismutase, catalases and peroxidases, thioredoxins, and peroxiredoxins. Superoxide dismutase effectively reduces the concentration of superoxide anions, enabling its transformation into oxygen or hydrogen peroxide [24]. When overproduced, oxygen radicals cannot be neutralised in sufficient quantities by enzymes. The supply of high oxygen concentrations may cause the accumulation of oxygen radicals and initiate oxygen toxicity known as oxidative stress.

Long-term exposure to high levels of oxygen in the breathing mixture has negative effects on the patient [27]. Hyperoxia leads to atelectasis [28, 29], but it can also cause other pulmonary complications, such as pneumonia [30] or hyperoxic acute lung injury [22, 31]. Hyperoxia also has an adverse impact on the functioning of the circulatory system, leading to a decrease in cardiac output and stroke volume, and an increase in systemic vascular resistance (SVR) [32, 33].

The decrease in cardiac output is due to both an increase in SVR and a decrease in heart rate. The effect of lowering the heart rate is related to the influence of hyperoxia on the predominance of the activity of the parasympathetic system [34]. The increase in SVR is associated with reduced nitric oxide (NO) production, which is inhibited by an increased amount of ROS [35]. The increase in vascular resistance also affects the coronary vessels, resulting in a decrease in coronary blood flow [36]. Mak *et al.* observed hyperoxia-induced impairment of cardiac relaxation [37].

Hyperoxia is associated with increased mortality among critically ill patients with traumatic brain injury (TBI) [38], stroke patients requiring artificial lung ventilation [39], cardiac arrest patients [40], and other groups of critically ill patients [41, 42]. In a follow-up study of a PROXI trial, ventilation with high concentrations of oxygen during abdominal surgery was found to be associated with increased mortality in cancer patients. Observations like this were not made in the group of patients without cancer [43].

Hyperoxia affects neural activity. High concentrations of oxygen decrease the cerebral metabolic rate of O₂ (CMRO₂) [44, 45]. It has been observed that hyperoxia suppresses the α and β bands of spontaneous neuronal activity [46]. Studies in animal models have shown that high oxygen concentrations reduce neurotransmission, particularly in the cerebellum and striatum [47]. Hyperoxia leads to impaired glucose transport across the blood-brain barrier (BBB) by inhibiting glucose transporters in the brain (primarily GLUT1), causing a decrease in glucose levels in the cerebrospinal fluid and in cells behind the BBB and causing local hypoglycaemia [48].

Hyperoxia increases the risk of non-traumatic acute brain injury [49]. A high oxygen concentration in the breathing mixture causes postoperative delirium [50]. Because it causes alterations in cerebral blood flow, hyperoxia is also associated with cognitive impairment and dementia [51]. It may also lead to secondary brain damage in TBI patients by increasing the concentration of glutamate in the brain tissue [52]. Hyperoxia is associated with increased mortality and worse outcomes among patients with TBI [53].

Due to the above observations, researchers emphasize the unfavourable effects of liberal oxygen therapy and are inclined to restrict oxygen dosing in critically ill patients [2, 54, 55].

It seems that ORi monitoring may be helpful in controlling high PaO₂ values during artificial lung ventilation. Yoshida *et al.* demonstrated that hyperoxaemia could be detected in patients under general anaesthesia by observing ORi values, which suggest what the correlating PaO₂ values might be [56]. Compared to the sole use of blood saturation monitoring, intraoperative monitoring of blood oxygenation by pulse oximetry with simultaneous measurement of the ORi enables the use of lower inspired oxygen concentrations, thus helping to avoid the risk of hyperoxaemia [57].

Contrasting findings have been obtained by de Courson *et al.* in a study conducted among ICU patients hospitalised for subarachnoid haemorrhage, haemorrhagic stroke, or ischaemic stroke. They found a weak correlation between the ORi and PaO₂. They speculated that their result was different because intensive care patients are exposed to factors such as the presence of peripheral oedema, the need to use catecholamines, and others, which potentially affect the reading of the signal by the ORi sensor placed on the patient's finger [58].

ORi in endotracheal intubation

Fleming *et al.* conducted a study to investigate the usefulness of the ORi as a tool for early detection of the risk of desaturation during endotracheal intubation [59]. They observed that during prolonged apnoea after endotracheal intubation, in cardiac surgery patients, the ORi signalled impending hypoxia an average of 48 s earlier than the standard pulse oximeter measuring blood saturation, and the median time from the ORi alarm to a 94% decrease in saturation (warning time) was 80.4 s. The median SpO₂ warning time was 29 s [59]. Similar results were reported in obese patients, in whom ORi monitoring provided an early warning of possible desaturation, although the period between the decrease in the ORi and desaturation was shorter in these patients compared to those with a BMI in the normal range [60].

Szmuk *et al.* conducted a similar study among 33 children with a mean age of 7.6 \pm 4.6 years. In this group of patients, the median time for the ORi to detect impending desaturation was 31.5 s before SpO₂ reached 90% [61].

In a study by Cheng *et al.*, the median time from an ORi alarm to a 90% drop in SpO₂ was 300 s. According to the authors, this prominently longer warning time was probably due to the longer pre-oxygenation of patients prior to intubation and the fact that the cohort consisted of healthier patients – 88% of the individuals enrolled in the study were ASA I or II patients [62].

Equally promising results were obtained by Yoshida *et al.*, who examined the ORi reaction time in rapid sequence induction (RSI). During RSI and endotracheal intubation, which was not preceded by face

mask ventilation, a decrease in the ORi was registered approximately 30 s before a decrease in SpO₂ [63].

Yoshida *et al.* also suggested that the ORi could be considered as an indicator of adequate preoxygenation in RSI. They claimed that the moment when the ORi reached a plateau could be the moment of maximum oxygenation of the patient, i.e. the optimal time to start RSI [63].

Hille *et al.*, in a NESOI study, demonstrated the usefulness of ORi monitoring in addition to monitoring blood saturation during endotracheal intubation in a group of intensive care patients. In their study, during apnoea, the decrease in the ORi below the predetermined threshold of 0.4 considerably preceded the decrease in SpO₂ below 97%; the median between these 2 time points was 81 s. In addition, those authors observed that in patients who had higher ORi values during pre-oxygenation, the risk of hypoxia during intubation was lower [64].

To sum up, earlier detection of impending desaturation may translate into greater patient safety in the operating room and contribute to the reduction of complications resulting from hypoxemia during RSI. This applies particularly to difficult airway patients. For this reason, the use of ORi monitoring in the perioperative period may significantly improve the safety of anaesthetised patients.

ORi in one-lung ventilation

The usefulness of ORi monitoring was also studied during one-lung ventilation (OLV) in patients undergoing thoracic surgery [65–69]. Koishi *et al.* demonstrated that there was a significant correlation between the ORi and PaO₂ during OLV. A decrease in the ORi during OLV was registered much earlier than a decrease in SpO₂. The mean time difference between the decrease in these parameters was 200 s. These results are consistent with other reports presented so far. Koishi *et al.* also observed that for a given PaO₂ value, ORi values varied between different patients; and vice versa – with the same ORi value, different patients had different PaO₂ values. Those authors suggested that the ORi could be a useful tool for the early detection of deteriorating blood oxygenation during one-lung ventilation [65].

Similarly, Sagioglu *et al.* found that the ORi could warn of impending hypoxia during OLV approximately 5–6 min before SpO₂ values began to decline. They noted that ORi monitoring was particularly useful in the initial period of anaesthesia up to 30 min after the initiation of OLV. By monitoring the ORi, the anaesthesiologist gains added time to prevent impending hypoxia [66].

Alday *et al.* also demonstrated that the ORi was particularly useful in predicting impending hypoxia at the beginning of anaesthesia. They observed that an ORi value of zero 5 min after the initiation of intubation predicted a high risk of hypoxia during OLV [67].

Monitoring the ORi during OLV enabled the use of lower concentrations of oxygen in the breathing mixture. As a result, patients with ORi monitoring had lower PaO₂ values than patients without additional ORi monitoring. Saraçoğlu *et al.* thus demonstrated that ORi monitoring could prevent the risk of hyperoxia in patients, and in this way shorten their postoperative stay in hospital [68].

Contrasting observations have been reported by Yang *et al.* They did not find evidence that ORi-guided adjustment of oxygen concentration in the breathing mixture allowed the use of lower FiO₂ during OLV. Such a possibility only arose during pulmonary vascular ligation, which may have been related to the reduction in the pulmonary shunt fraction. The authors did not observe any significant differences in the incidence of hyperoxia, hypoxia, or pulmonary complications between the ORi group and the control group. However, they pointed out that their study might have been limited by the small size of the patient groups and an excessively high target ORi value adopted in the experiments [69].

Further perspectives for ORi measurement in critically ill patients

Research published so far indicates the significant usefulness of ORi as one of the parameters for monitoring the body's oxygen metabolism.

The possibility of using the oxygen reserve index for detecting patients requiring prolonged pre-oxygenation who have not increased their oxygen reserves within a standard time seems to be particularly important. This applies to critically ill patients requiring intubation during treatment in an intensive care unit, as well as patients undergoing general anaesthesia in elective surgeries or patients in emergency departments [64].

ORi, as a continuously monitored parameter, may contribute to shortening the time of unrecognized hyperoxia among critically ill patients who receive too much oxygen in the respiratory mixture. ORi monitoring could reduce the frequency of follow-up blood gas tests and the need for frequent blood collections [70].

It is also worth monitoring the oxygen reserve index to detect impending hypoxia, which gives the anaesthesiologist more time to take preventive measures before a drop in SpO₂ occurs [16, 17, 19, 20].

Limitations of ORi

Despite the numerous possibilities of using ORi monitoring in both anaesthesiology and intensive care, one should not forget about the limitations of this method.

There are reports that after intravenous injection of indigo carmine, ORi values temporarily decrease. This may falsely warn clinicians of impending hypoxia [71].

Of course, similarly to pulse oximetry, the ORi may not read when peripheral perfusion is impaired.

In addition, the ORi may be affected by PaCO₂, pH, or temperature [14, 67].

As mentioned previously, ORi values range between 0.00 and 1.00. This parameter does not have negative values, which may make it difficult to detect hypoxia in certain settings. Therefore, simultaneous use of the ORi and SpO₂ as complementary parameters is recommended.

Conclusions

ORi monitoring is a simple, quick, and versatile tool that allows clinicians to predict both impending hypoxia and hyperoxia, giving them time to take appropriate action.

Studies on the use of the ORi in clinical practice have shown promising results, but further research with large study groups is needed to confirm them.

Conflict of interest

The author declares no conflict of interest.

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